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THE
PHYSIOLOGICAL AND THERAPEUTICAL ACTION
OF
ERGOT.

BY
ETIENNE EVETZKY, M.D.

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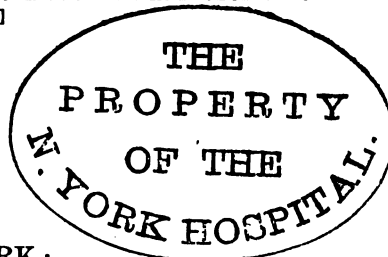
BY

ETIENNE EVETZKY, M. D.

"L'ergot de seigle est un médicament dont on n'a certainement pas encore tiré tout le parti qu'on en doit attendre."

"Bull. Gén. de Thérap.," xxxiii, 1847, p. 163.

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P R E F A C E .

EVERY one familiar with the history of medicine will acknowledge that the system of therapeutics of a given period is the logical outcome of the pathological ideas of the day. During the reign of the humoral pathology, when disease was considered to be due to some change or impurity of the blood, the indication was invariably to cleanse the system or to modify the blood. To obtain these results, the treatment consisted in the use of alteratives, purges, diuretics, expectorants, emetics, emmenagogues, counter-irritants, etc. At the time of the appearance of Virchow's "Cellular Pathology," the progressive portion of the profession had become utterly tired of the metaphysical, fanciful, and totally untenable pathological ideas constituting humoralism, and of the therapeutic methods resulting from them. The reaction gave rise to the motto, "Hands off!" The profession, like a man suddenly transferred to entirely new surroundings, had taken a very undecided and wavering stand with regard to therapeutics. The former attempts at radical cure, or at reaching the essential nature of the disease, were abandoned; where it was practicable, the disease was allowed to follow its course; treatment, in fact, assumed an essentially symptomatic, expectant, and palliative character, retaining, of course, the empirical facts obtained during centuries of practice. Under the healthful influence of the revolution inaugurated by Virchow, the study of the action of remedies received new life, while pathology was steadily resolving itself into a gradually diminish-

ing number of ultimate morbid processes, the nature of which was becoming clearer and clearer. After nearly half a century of this combined work, these two streams, formerly parallel, began to converge, and, being at first separated by a vast space, they are now to be seen at a glance, and readily connected with each other. Having reached this stage, we have acquired a solid foundation to build rational therapeutics upon. We appreciate the complexity of disease and the limitation of our curative powers; in this we differ from our colleagues of past centuries; but, on the other hand, we find that the empiricism and the methods of expectancy and non-interference, in vogue some years ago, have outlived their time. We realize that we must be rational in the use of drugs when we can, and empirical only if we must, and that we possess greater power in dealing with disease than was conceded not a very long time ago. The position of ergot in this respect is particularly favorable. The chemical composition and the physiological properties of this drug are well understood, while the morbid conditions referable to the latter are readily pointed out.

It seems strange, then, that in none of the leading works on therapeutics the uses of ergot in disease have been treated with proper completeness and system. In undertaking the present work my object was to present in a condensed manner all the therapeutic possibilities of ergot. In a task of this nature, original research is out of the question. No one man's evidence is sufficient to establish the merits of a drug considered in the manner indicated, and no one man's opportunities are sufficient to grasp the entire subject. Consequently it remained to gather from the volumes of past and current periodical literature the testimony of the multitude of physicians that had been led to use ergot in different morbid conditions. I have recorded everything that has come to my notice; I have grouped and classified the immense material in our possession. In all cases in which the action of ergot could be explained, I have attempted to do so, although this task is frequently difficult, if not impossible. I have pointed out some properties of ergot which are

not apparent when we study its physiological action or its toxic effects. This difference between the action of drugs in the normal and morbid conditions of the system is not sufficiently appreciated, and we still labor under the impression that we obtain a perfect insight into the therapeutic possibilities of a remedy from the manner in which it affects the system in health. The reader will see that ergot has been used in a large number of diseases; some of these uses have little or no practical value, yet it is very important to know them, as they serve to illustrate the therapeutic properties of the drug. They have been brought to the notice of the reader without any comments, but those that are essential and of the greatest practical importance have been dealt with more fully. Among the latter may be mentioned the use of ergot in inflammation, aneurism, cardiac diseases, the post-parturient state, uterine fibroid tumors, rheumatism, etc.

This work was published at first *seriatim* in the "The New York Medical Journal and Obstetrical Review," and is now issued in book form, to place it within the reach of the profession at large.

E. E.

NEW YORK, 1882.

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THE
PHYSIOLOGICAL AND THERAPEUTICAL ACTION
OF
E R G O T.

PART I.

E R G O T.

SYNONYMS.—Ergota* (U. S. and Br. Ph.), ergot, ergot of rye spurred rye, cockspur rye, etc.; *Fr.*: ergot, ergot de blé, ergot de seigle, seigle ergoté, etc.; *Ger.*: Mutterkorn, Ergot.

HISTORY. †—Undoubtedly our first knowledge of the medicinal virtues of ergot was obtained at the price of numerous epidemics of ergotism which visited Europe in the early ages after seasons of rain and scarcity. The information we have in relation to the earliest epidemics permits us only to assume that they were ergot diseases. But as to later ones, beginning with the tenth century, we can positively identify the usual forms of ergot poisoning in the description given. Dangerous properties of ergot became known quite early. According to Mézeray, Sigebert de Gremlour pointed out, in 1096, the connection of epidemics with the abundant presence of ergot in rye. It is impossible to indicate at what period ergot began to be used for medicinal purposes. The earliest references show that

* In French, *ergot* signifies cockspur.

† Stillé, "Therapeutics and Materia Medica," vol. ii, p. 717, Phila.; S. Wright, "Edinburgh Med. and Surg. Jour.," lii, p. 293, liii, p. 1.

some of its virtues were known already to the masses, and that it was used extensively in obstetric practice. Such a statement is made by Adam Lonicer, of Frankfort, who lived toward the middle of the sixteenth century. In 1576 the Medical Academy of Marburg attributed to this substance a spasmodic disease which then prevailed in Hesse. Johannes Thalius (1588) speaks of it as used "*ad sistendum sanguinem*." Camerarius (1688) refers to its use by German midwives. In 1693 the English botanist Ray described some of its medicinal properties. In France, according to Borden, it was used from time immemorial to increase uterine action. Barlurdini, Laneri, and Amaretti state that it was used in difficult labor. Parmentier (1774) refers to the same with regard to Alsace.

In the course of the eighteenth century allusions to ergot are met with more frequently. It was used mainly among the lower classes, but still more extensively by charlatans, with criminal intent. This led to its use being interdicted in France in the year 1774. Toward the close of the last century, although still favorably indorsed by some physicians, it lost almost entirely the little reputation it had had. But in the beginning of the present century, mainly by the efforts of the American physicians, it was again revived. Drs. Stearns (1807), Akerly, Prescott (1813), Chapman, Dewees (1817-1818), and Atlee (1821) largely contributed to turn the tide of professional opinion in its favor; but European physicians presented a considerable opposition, Chaussier and Madame La Chapelle being most prominent in combating the idea of its efficiency. The contributions of Bogeschi, Davis, Michell, Villeneuve, and others finally resulted in removing the opprobrium attached to it.

Ergot was admitted into the London Pharmacopœia in 1836. Then a thorough study of its physiological action was entered upon, and as the work progressed the field of the therapeutic usefulness of ergot was extended; but the latter did not keep pace with the former, and, even at the present day, although we possess the essential knowledge of its physiological action, we greatly underestimate its therapeutic value.

BOTANY.*—Ergot is the second stage in the evolution of a biennial fungus, named by Tulasne (1853) *claviceps purpurea*. This middle stage forms the sclerotium which occurs in a large number of the most various fungi, and is a special state of rest of these plants. Almost all our knowledge of the subject is due to the researches of Tulasne. This fungus usually infects rye, but all the graminaceæ are apt to suffer from it, also the cyperaceæ, and, perhaps, the palmaceæ. Although rainy seasons are most favorable for its development, dampness is not absolutely necessary. The formation of ergot takes place only in a few, usually from three to twelve, caryopsides in an ear, but more may be diseased. The first sign of ergot development is the appearance of the so-called honey-dew of rye—a yellowish mucus having an intensely sweet taste and the peculiar disagreeable odor often belonging to fungi. These drops attract ants and beetles, which have been supposed to be instrumental in the development of ergot. The honey-dew substance, treated with oxide of copper, shows the presence of sugar, which is probably the result of the decomposition of starch by the fungus. Examined under the microscope, it is found to contain an immense number of conidia. The drops dry up in a few days, and the ergotized soft ovaries become covered with and penetrated by a white spongy tissue—the mycelium of the young fungus. It is made up of slender thread-like cells, the hyphæ, the outer layer of which consists of rapidly-diverging cells, the basidiæ. Ergot, in this primary or mycelium stage, was regarded as an independent fungus by Lévillé (1827), who named it *sphacelia segetum*.

The second stage begins with the mycelium penetrating and enveloping the caryopsis, with the exception of the apex, and thereby preventing its further growth. At the base of the caryopsis there is formed, by tumefaction and gradual transverse separation of the thread cells of the mycelium, a more compact, kernel-like body (the future ergot), violet-black without, white within, which gradually but largely increases in size, and ultimately separates from the mycelium as the loose tissue of the latter dries up and shrinks after

* F. A. Flückiger and D. Hanbury, "Pharmacographia," London, 1874, p. 672.

the completion of its function. By this growth the remains of the caryopsides, still recognizable by their hairs and by the rudiments of the style, become visible above the paleæ on the apex of the mature ergot, now projecting prominently from the ear. In the commercial drug the apex is usually broken off.

It is evident that, in the process of development just described, the tissue of the caryopsis of the rye does not undergo a transformation, but that it is completely destroyed; and the microscopic structure of the ergot does not exhibit any resemblance to a caryopsis or a seed. De Candolle (1816) considered the fungus complete, and named it *sclerotium clavus*; and Fries, *spermœdia clavus*.

Nothing further occurs in the ergot while it remains in the ear, but, laid on damp earth, after some months of rest in the succeeding spring, at certain points small orbicular patches of rind fold themselves back and throw out little white heads. They increase in size, assume a grayish-yellow color changing to purple, and finally, after some weeks, stretch themselves toward the light on slender, shining stalks of a pale violet color. The stalks often attain an inch in length, with a thickness of about half a line. After a short time there appears on the surface of the head a number of brownish warts, in which are the openings of minute cavities composed of a large number of sacs, each containing, as is usual in fungi, eight spores. The total number of spores in the twenty or thirty heads sometimes produced from a single ergot often exceeds a million. These heads represent the true fructification of the fungus, and they die in two or three weeks from the time of their appearance. This state of the plant appears to have been observed for the first time in 1801, by Schumacher, who called it *sphœria*; other names were given it, until Tulasne proved it to be the final stage of the development of ergot. The three different forms of this fungus—namely, the mycelium, the ergot, and the fruit-bearing heads—are, therefore, merely successive states of one and the same plant, the *claviceps purpurea*.

DESCRIPTION.—Ergot as found in commerce consists of fusiform grains. They are from one third to one and a half inches long, and

from one half to four lines in diameter, subcylindrical or often obtusely triangular, tapering at both ends, usually somewhat curved, with three longitudinal furrows and an easily-detached, small, yellowish appendage or head at the apex, while the opposite extremity is somewhat rounded. The ergots are firm, horny, somewhat elastic, have a close fracture, are brittle when dry, yet difficult to pulverize. They are externally of a purplish-black color, the surface frequently fissured transversely; internally, whitish with purplish, striæ, of a uniform texture. The tissue is imperfectly penetrable by water, even the thinnest sections swelling but slightly. It has a peculiar, unpleasant odor of spoiled fish, and a mawkish, oily, acrid taste.

MICROSCOPIC STRUCTURE.—Fully-developed ergot consists of uniformly densely-felted tissue of short, thread-like, somewhat thick-walled cells, which are irregularly packed and so intimately matted together that it is only by prolonged boiling of thin slices with potash and alternate treatment with acids and ether that the individual cells can be made evident, the aspect of which differs from that of the hyphæ of other fungi in being shorter, containing numerous drops of oil, but neither starch nor crystals; otherwise they are empty. Some of the cells of the outermost rows are of a violet color, and their walls are thicker.

VARIETIES OF ERGOT.—The foregoing description applies to the ergot of rye, but the fungus can attack other plants, producing ergot similar in all essential points to the ergot of rye. *Ergot of wheat*, collected in some parts of France and Italy, differs from the latter, being shorter, thicker, harder, and having a less disagreeable odor. It is more easily preserved; medicinally it is similar to rye ergot. According to Carbonneaux Le Perdriel, it is free from some of the unpleasant effects peculiar to rye ergot. Mialhe and Grand Clement recommend it in preference to the latter, while Pouchet and Jobert pronounce them to be identical in their therapeutic effects. *Ergot of oats* is more slender than that of rye. *Ergot of maize*, according to Jobert, is identical in medicinal virtues with rye ergot. *Ergot of diss* (arundo ampelodesmos, Cirillo—a North African grass), according to Lallemand, is twice as strong as ordi-

nary ergot. It is of the same internal structure, but longer and not so thick.

PRODUCTION, COLLECTION, AND COMMERCE.—Ergot is found all over Europe, and also in this country, but not in as great quantities in all places. It is the most common in countries where agriculture is conducted on the most primitive principles. The ergot harvest is more abundant in damp, rainy years. The countries from which it is most largely exported are Russia, Spain, certain parts of Austria, Italy, and France. In the central parts of Europe ergot is so scarce that its collection is not profitable. The same may be said also of this country, as all the ergot used here is imported. According to Wood, the United States were entirely free from ergotism. It is found most extensively on the borders of the fields, where the wind carries the spores more readily. Honey-dew drops are inactive, and are collected in Russia by the children and eaten by them with relish.

Ergot must be gathered from the ear a little before the harvest, and if picked too early it is entirely inactive, or is very feeble. According to Bonjean, the active properties do not appear before the sixth day. Besides, the strength of ergot varies with the crop and the locality.

The consumption of ergot is rapidly increasing. In England during 1839 the importation of ergot was one and a half tons; the wholesale price of it during 1825-'28 varied from twenty-six to fifty shillings a pound. The importation of ergot into this country during 1876-'77 was ten times greater than during 1866-'67. How rapidly it increased can be seen from the following table, kindly furnished me by J. Nimmo, Jr., Chief of the Bureau of Statistics, Treasury Department. It gives the quantity, value, and average cost by the pound of ergot imported into the United States during the fiscal years ending June 30, 1870-'79, inclusive.

YEAR ENDING JUNE 30.	Pounds.	Value.	Average Cost a Pound.
1870.....	16,177	\$6,723.18	41.0 cents.
1871.....	17,804.5	6,898	38.0 "
1872.....	29,480	10,094	34.0 "
1873.....	45,347	11,784	26.0 "
1874.....	31,304	4,561	14.5 "
1875.....	60,620	10,878	17.9 "
1876.....	42,599	15,192	35.6 "
1877.....	75,550	47,738	63.0 "
1878.....	63,804	14,797	22.7 "
1879.....	81,508	16,126	19.8 "

PRESERVATION.—Ergot is a substance very hard to keep. The fixed oils forming an important constituent of it become rancid with the free access of air. It is also apt to be attacked by an insect—a mite of the genus *trombidium*. Ergot is more readily deteriorated in the form of powder; but, if closely shut up in dry bottles, it can be kept for a considerable time. A little cotton soaked in chloroform, or a bit of camphor, will protect it from the insect. Viel* recommends pulverizing the ergot with sugar. Ducroc† advises placing on ergot some powdered wood charcoal (oak or pine). Mourral‡ speaks highly of the the preserving power of benzoin. He mixed with the pulverized ergot 5 per cent. of powdered benzoin, and found the ergot fourteen months later to possess its original strength. This method is indorsed by a number of French physicians. Still, the strength of ergot is uncertain if it is more then a year old.

DETECTION OF ERGOT.—Although, according to Bonjean, ergot loses its poisonous properties to a considerable extent if taken in bread, still this is the only means of poisoning, except when taken for medicinal purposes. The peculiar color and odor of flour and bread (according to Orfila, the latter has dark, violet-colored spots) are usually sufficient to reveal its presence. But, if its amount is not great, chemical manipulations will be required for its detection. The test of Winkler is old and unreliable, because, according

* "Am. Jour. of the Med. Sci.," 1852, p. 556

† "New Remedies," 1875, p. 156.

‡ "Jour. de Thérap.," May, 1876.

to Dragendorff, caustic potassa generates trimethylamine with other substances also. It consists in mixing the suspected substance with the solution of KHO; this is heated, and a peculiar penetrating odor of herring is generated, indicating that ergot is present in a larger amount than 1.5 per cent. The test of Zinin,* improved by Jacobi, is more reliable and delicate. The suspected flour is boiled in the 85-per-cent. alcohol for the purpose of extracting from it different coloring substances which may interfere with the test. A given amount of flour, say 10 grammes, is treated twice with 30 grammes of the boiling alcohol of the same strength. The solution is filtered and the flour is expressed and put into a test-tube into which is poured 10 grammes of cold alcohol. If the alcohol on repeated agitation remains of the natural color, 20 drops of diluted sulphuric acid (1.5) is added to it. If the flour contains ergot, the fluid will assume a beautiful reddish-pink color, by the intensity of which we can judge of the amount of ergot in the flour. The method of Rakowitch, as modified by Kaplanowsky, is as follows: 4 grammes of flour is placed in a small wineglass containing 24 c. c. of chloroform and 7 c. c. of 95-per-cent. alcohol. The glass is corked, thoroughly shaken, and its contents allowed to settle. The flour will fall to the bottom of the vessel, while the ergot will rise to the surface in the form of fine, black particles, mixed with a small amount of bran. According to the report of the commission appointed by the Russian government in 1864, flour containing but one per cent. of ergot produces very dangerous symptoms, and the amount of it is frequently much greater. In the epidemic reported by Swjatlowsky† the flour contained seven per cent. of ergot.

CHEMICAL COMPOSITION.—From the fact that ergot is but an agglomeration of fungi, low organizations, it is natural to assume that its composition will be complicated and not very stable. This is the reason why the chemists have had so much difficulty in determining its component parts; and, although we possess at present a pretty accurate idea of its composition, still there are some uncertainties for future examiners to determine.

* "Meditz. Obozrenie," xvi, 1881, p. 266.

† "Vratsch.," 1880, Nos. 10 and 11.

The ingredients composing ergot may be divided into the active and the indifferent. To the latter belongs a *fatty substance*—a yellowish, bland, non-drying fixed oil. Its specific gravity is 0.925. With soda and potash it is easily saponified. It is composed of oleine, 69.2 per cent.; palmatine, 22.7 per cent.; glycerides, 8 per cent.; and a small amount of volatile fatty acids. The decomposition of ergot is due to the oxidation of this fatty substance, and after the oil is extracted ergot is more readily preserved. If obtained by expression, it is free from any poisonous or irritating properties, but, if extracted with ether, it is irritating and poisonous, on account of the presence of *resin* and active principles of ergot.

Fat forms about 30 per cent. of the crude drug. *Cholesterine* is found in it at times, but it may be wanting. If present, it is always in a small amount—about 0.036 per cent. It was first noticed by Stahl (1865), but its nature was defined by Schoonbroodt (1866), and Ludwig (1869). Its presence was also confirmed by Ganzer.

Mycose is found in ergot, one part in 1,000. It crystallizes in rhomboid prisms, and melts at a high temperature, giving off a decided odor of caramel. It is not as sweet as cane sugar, and polarizes light to the right three times more than the latter. Its formula is $C^{12}H^{22}O^{11} + 2H^2O$.

Lactic acid and its salts were found in ergot by Schoonbroodt in 1866. Buchheim and others believe they are derived from the mycose by the action of the ferment of ergot upon the latter.

Fungus cellulose, or *fungine*, differs from the ordinary cellulose in the fact that the usual reactions with iodine and sulphuric acid are wanting.

Mannite was found by Mitscherlich, Fiedler, and Ludwig, in place of mycose.

Leucine was found by Buchheim, but he is not certain if this substance is a normal constituent of ergot or an artificial product.

Methylamine, according to Ludwig, is a normal component part of ergot, but its presence is denied by Manassewitz and Ganzer,

while Tanret thinks that it is derived from the decomposition of his ergotinine.

Trimethylamine is obtained by heating ergot with any caustic alkali, when its characteristic odor is evolved, serving for the detection of ergot. It was first described by Winkler. The general opinion in regard to these two substances, and also *ammoniacal salts*, is that they are the products of decomposition.

Formic and *acetic acids* are also found in ergot.

Albuminoid substances are present to the extent of 3.09 per cent., according to Thielon, and 3.2 per cent., according to Ganzer.

The following mineral substances have been found in the ashes of ergot: *Phosphoric acid* (13.25–50.5 per cent.), *potash* (18–39 per cent.), *soda* (0.65–14 per cent.), *lime* (1.25–1.50 per cent.), *manganese* (2–4.75 per cent.), *oxide of iron* (0.70–2 per cent.), *silica* (2.5–14.5 per cent.). Some have also found *alumina* (0.3–0.6 per cent.), *oxide of manganese* (0.25–4 per cent.), *oxide of copper* (0.5 per cent.), *sulphuric acid* (0.02 per cent.), *chlorine* (2–2.5 per cent.), *carbon* (12.1–12.6 per cent.), *chloride of sodium* (0.6–1.5 per cent.).

According to Buchheim, there is no *starch* in ergot, although its presence was claimed by Schröder and Legrip. The same authority denies the existence of *gum* and *vegetable mucine*. The coloring matter was first spoken of by Sage, in 1776. According to Dragendorff and Podwissotzky, it is composed of two substances, both intimately connected with lime—*sclererythrine* and *sclerojodine*.

Sclererythrine is extracted from ergot by a solution of tartaric acid. It is not soluble in water, but is soluble in alcohol, in ether, in chloroform, and, particularly, in caustic potash, ammonia, etc. The solution of *sclererythrine* in an alkali has a beautiful murexide color; with sulphate of aluminium and chloride of zinc, the alcoholic solution assumes a red color. With the salts of borium, calcium, and many heavy metals, it gives a blue precipitate. *Sclererythrine* stands in a near relation to *chrysophanic acid* and *alizarine*. Its quantity in the mature ergot varies from 1 to 2 parts in 100,000. It is not an entirely inert substance.

Sclerodine is obtained at the same time with the preceding. It is not soluble in water, alcohol, ether, or chloroform. With potash it assumes a beautiful violet color, from which it can be precipitated by acetic acid. Concentrated sulphuric acid dissolves sclerodine, assuming a blue-violet tint; thence its name. Sclerodine is found in ergot in the proportion of 1 to 1,000. It has also slight active properties resembling those of the preceding.

Dragendorff and Podwissotzky found in ergot two crystallizable substances—*sclero-crystalline* and *sclero-xanthine*, both perfectly inert. The first presents itself as almost colorless needles, insoluble in water, alcohol, or ether, but soluble in caustic potash and ammonia. The probable formula is $C^{10}H^{10}O^4$. The second is the hydrate of the first, and appears as yellow crystals. Its probable formula is $2C^{10}H^{10}O^4 + 3H^2O$.

The above-named ingredients form the bulk of the crude drug, but do not determine its specific effects, which are produced by the substances to be spoken of presently.

The attention of the profession was called to the active principles of ergot by Wiggers,* in 1830, when he described his ergotine—a substance of brownish color, slightly soluble in alcohol, but not in water or ether. He obtained it by first extracting the fats by means of ether, then heating the residue with alcohol, and evaporating it, when it was washed repeatedly with water. In 1842 Bonjean† presented his extract, which differed in some respects from the former, being an aqueous instead of an alcoholic extract. He treated the powder first with water, to which he added half its weight of alcohol to precipitate certain ingredients held in solution; this was then filtered and evaporated. Bonjean's extract is officinal in many continental pharmacopœias under the name of *extractum ergotæ*, s. *secalis cornuti*.

In 1864 Wenzell‡ stated that the active properties of ergot were due to two alkaloids—*ergotine* and *ecboline*, and a crystallizable volatile acid—*ergotic acid*, with which they were combined. These alkaloids differed from each other in many respects. Ecboline was

* "Ann. der Pharmakol.," i, p. 129.

† "Comptes Rendus," xiv, p. 899.

‡ "Am. Jour. of Pharm.," 1864, p. 193.

precipitable by corrosive sublimate, and acted mainly on the brain and muscles; while ergotine could be precipitated by phosphomolybdic acid, was less active, and affected mainly the circulation. Both were brownish, had a bitter taste, were uncrystallizable, soluble in water, alcohol, and ether. Manassewitz* confirmed the presence of ergotine, whose formula he defined as $C^{50}H^{52}N^2O^3$, finding it in the proportion of 0.12 per cent. But he could not find either ecboline or ergotic acid. In 1870 Ganzer† and Hermann‡ confirmed the analyses of Wenzell. Ecboline, according to Ganzer, was found in the proportion of 0.16 per cent., and ergotine in that of 0.04 per cent. He obtained also hydrochlorate of ergotine, crystallizable in needles. In 1871 Haudelin# stated also that the active properties of ergot were due to an alkaloid. In 1872 Wenzell|| described a modification of his process. In 1874 Buchheim^ proved that Wenzell's alkaloids were not alkaloids, and, moreover, were not pure compounds, and, as an active ingredient, he pronounced a substance similar to Wiggers's ergotine—a dark, colloid substance, very hygroscopic, and of acid reaction. The same year Wernich◇ stated that the active principle of ergot was an acid soluble in water, but not in absolute alcohol. Zweifel‡ thought that the active principle of ergot must be an alkaloid, but that Wenzell's alkaloids were not the ingredients, because after they were precipitated by tannic acid and corrosive sublimate the solution still contained some active properties. Tanret,♯ in 1875, extracted from the fixed oil of ergot, treated with ether and acidulated water, an alkaloid which he called ergotinine. It is crystallizable at first, but soon becomes resinous. One kilogramme of fresh ergot yielded but 1.20 grammes of the

* "Pharm. Ztschr. f. Russland," 1867, p. 387.

† "Arch. f. Pharm.," etc., xciv, p. 195.

‡ "Viertelj. f. prakt. Pharm.," xviii, pp. 4, 81.

"Einige Beiträge zur Kenntniss des Mutterkornes," Diss., Dorpat.

|| "Arch. f. Pharm.," etc., cc, p. 256.

^ "Arch. f. exp. Pathol. u. Pharm.," iii, p. 1.

◇ "Einige Versuchsreihen über d. Mutterkorn," Berlin, 1874.

‡ "Arch. f. exper. Pathol. u. Pharm.," 1875, p. 387.

♯ "New Remedies," 1878, p. 206; "Répertoire de Pharm.," 31^{me} année, n. s., iii, p. 708.

alkaloid, and only one third of this was in the form of crystals. Its formula is $C^8H^{10}N^1O^6$.

It is apparent from the foregoing that some only succeeded in partially isolating the active ingredients, while others were led astray by almost insurmountable difficulties in separating them, and obtained only artificial complex compounds. From the latest works (Buchheim, Wernich, Zweifel, and others) it is evident that more appropriate methods have been adopted, as their results correspond more closely with those of Dragendorff and Podwissotzky,* who gave us a positive knowledge of the active ingredients of ergot. They are sclerotic acid and scleromucine.

Scleromucine is a slimy, colloid substance, soluble in water and precipitable by forty- to forty-five-per-cent. alcohol. It is darker than sclerotic acid, slightly hygroscopic, inodorous, and tasteless. It is not a glucoside, an albuminoid, or an alkaloid substance. It contains nitrogen. When once dried it dissolves in water with the greatest difficulty. It is precipitable by tannic acid and phosphomolybdic acid. Scleromucine is found in the crude drug to the amount of two to three per cent. Dragendorff and Podwissotzky do not recommend its use, on account of its slight solubility in water when once dried.

Sclerotic acid is also a colloid substance, has marked acid properties, is soluble in water, forty-five-per-cent. cold alcohol, and seventy-five-per-cent. boiling alcohol. It is precipitable by eighty-five- to ninety-per-cent. alcohol, in combination with lime mainly, also potash, soda, silica, and manganese. It is of a yellowish-brown color, has no taste or smell, is slightly hygroscopic without being deliquescent. It does not possess any properties indicating it to be an alkaloid, except that it is precipitable by phosphomolybdic acid in the form of a yellow, and by tannic acid in the form of a colorless, mass. It can not be grouped with either albuminoid or glucosidal compounds. The qualitative and quantitative analytical methods are the same for both. Sclerotic acid is a compound of 3 to 4 per cent. of ash, 40 per cent. of carbon, 5.2 per cent. of hydrogen, 4.2

* "Pharmac. Jour. and Trans.," 1876, p. 1,001; "Arch. f. exp. Pathol. u. Pharm." vi, p. 153.

per cent. of nitrogen, and 50·6 per cent. of oxygen. Its formula is $C^{12}H^{10}NO^8$ or $C^{12}H^{10}NO^{10}$.

Sclerotic acid is found in ergot in the proportion of 3 to 4 parts in 100. Subcutaneous injections of 0·02 to 0·04 gramme produce gradually in frogs a state of complete palsy lasting from six to seven days. By its properties it is unusually well adapted for therapeutical uses. The dose for man is from 0·04 to 0·05 gramme. Dragendorff and Podwissotzky claim that it does not irritate the cellular tissue. Nikitine,* who experimented considerably with sclerotic acid, states that the injections are painful, but that they do not produce any local inflammation. He finds that sclerotate of soda is less active than the acid itself, and he also recommends the acid for therapeutical uses, as it possesses all the virtues of the crude drug.

In connection with this subject I may state that Levy,† on the basis of a few experiments (on three bitches and two pregnant women), recently asserted that the specific effects of ergot were due to the presence in it of phosphoric acid, which, according to him, acts like ergot in the conditions indicating the use of the latter. He states that the strength of ergot is in proportion to the phosphoric acid it contains.

The method of obtaining sclerotic acid and scleromucine adopted by Dragendorff and Podwissotzky is as follows: Powdered ergot is treated first with ether and absolute alcohol; then it is digested with water, and the solution is dialysed. The dialysate is afterward evaporated to a sirupy consistence, and a sufficient quantity of alcohol is added to it to bring its strength to 40 to 45 per cent.; this precipitates phosphates. Then more alcohol is added to raise its strength to 75 to 80 per cent., which will precipitate the salts of sclerotic acid, as they are not soluble in alcohol of this strength. The precipitated salts are purified by repeated washing in alcohol of this strength, and are redissolved in 45-per-cent. alcohol. At this stage the salts give 19 per cent. of ash. For the purpose of separating the acid from the bases, hydrochloric acid is added to the solution, and, to isolate sclerotic acid again, absolute alcohol is added.

* Rossbach's "Pharmak. Untersuch.," iii; "London Med. Record," March, 1879.

† "Am. Jour. of the Med. Sci.," 1876, p. 266.

Now the acid gives only 3 per cent. of ash, composed mainly of silica, manganese, phosphate of iron, and potassium. The dark liquid remaining on the dialyser, when mixed with sufficient alcohol to bring its strength to 45 to 60 per cent., yields scleromucine as a precipitate.

PART II.

THE PHYSIOLOGICAL ACTION OF ERGOT, AND TOXICOLOGY.

LOCAL ACTION OF ERGOT.—Ergot, according to Mialhe, has no chemical effect on *tissues*, except that of coagulating albumen. Applied to the *skin*, protected by the epidermis, it does not produce any apparent effect. But on raw surfaces, wounds, and abraded skin, it acts as an irritant, and very soon induces an unhealthy suppuration, and at times even mortification. Introduced *under the skin*, it leads to the formation of abscesses containing ill-smelling pus. The crude drug alone acts in such a manner; ordinary extracts properly diluted are nearly bland. Applied to *bleeding surfaces*, it stops the hæmorrhage. If a small quantity of the powder be taken into the *mouth*, its acrid taste and irritant properties tend to increase the flow of saliva, soon replaced by a feeling of dryness in the throat. In the *alimentary canal*, ergot in small doses does not produce any appreciable effect; but, if larger quantities (20–30 grains) be taken for any length of time, the feeling of dryness will be more marked, to which is added a sensation of constriction; salivation is increased, yet the thirst is very marked. Digestion is soon disturbed—the tongue is coated; the patient suffers from nausea, eructations, and vomiting; an oppressive feeling in the epigastrium is complained of; and frequently diarrhœa sets in. If still greater quantities be taken, as in the cases of criminal use of the drug, we find the mucous membrane of the entire alimentary canal, particularly that of its upper part, very much injected, and even spots of erosion may be present. In the *cellular tissue* the extracts, and also sclerotic acid, produce pain, sometimes inflammatory swellings running into suppuration, but more com-

monly temporary indurations with the signs of irritation. Of course in this case, as with all remedies, the extent of the local process depends greatly upon the state of the vitality of the tissues. The pain caused by the hypodermic injections is due, according to Buchheim, to the acidity of the fluid, and it is well to neutralize it. The *muscular tissue* is less apt to give these unpleasant results, and for this reason it should be the favorite place for the hypodermic administration of ergot. Ergot is at times given by the *rectum*, and, as a rule, it is borne well, only occasionally suppositories cause a feeling of burning. If they are introduced late in the evening, patients suffering from sexual debility are apt to have seminal emissions.

SYSTEMIC EFFECTS OF ERGOT.—The experiments of Schrübler and Zeller* would tend to indicate that ergot has a poisonous action on vegetable and also on the lower forms of animal life. According to Nikitine, † cold-blooded animals are affected by ergot more than warm-blooded animals. The herbivora show greater tolerance of it than the carnivora (Wright, ‡ Nikitine). Block# gives numerous instances of cows and sheep consuming enormous quantities of ergot for a long time with impunity, which may be due to the presence of tannic acid in the food. Its systemic effects depend upon the quantity taken and the length of time the system has been subjected to its influence. We will study first the general manifestations as seen in cases of poisoning, and then examine in detail and separately the specific actions of ergot on different organs and functions.

TOXICOLOGY.—Usually two forms of ergotic intoxication are described—the acute and chronic varieties; but in the case of man three forms of ergotism should be distinguished—acute, sub-acute or spasmodic, and chronic or gangrenous ergotism.

ACUTE ERGOTISM.—This can best be studied in *animals*, after injecting some fluid preparation of ergot into the blood-vessels. S. Wright states that immediately there are noticed dilatation of the pupils, great increase of the pulse rate, hurried respiration, evacuation of urine and feces, a fall of temperature, unconsciousness, an-

* Pereira, "Materia Medica and Therapeutics," Phila., 1854, ii, p. 136.

† *Op. cit.*

‡ *Op. cit.*

Pereira, *op. cit.*

æsthesia, and various motor disturbances, such as convulsions, paralysis, tetanus, and tremulousness—the animal dying rapidly with the symptoms of general paralysis. If a very large quantity of ergot be introduced into the stomach, the phenomena of poisoning develop more gradually and are less intense. In this case there are superadded also symptoms of local irritation—vomiting, diarrhœa, etc. A small quantity produces at first excitement, followed by depression, from which the animal, as a rule, recovers entirely. In view of the importance of this topic, I will transcribe the description of Wright's Experiment IV :

A solution furnished by half an ounce of ergot was slowly injected into the femoral vein of a large bull-terrier bitch weighing twenty-three pounds. About half an ounce of the fluid was propelled at once, to each of which injections the system answered by very increased arterial action and quick, hurried respiration. The first injection also produced violent convulsive movements of the whole body, but the hind legs were chiefly affected. The urine and fæces flowed abundantly, and the animal cried in a plaintive and agonized tone. The convulsions lasted for about three minutes, when the dog became still, the whole frame relaxed, being totally insensible to pain. The pupil was dilated and motionless, the action of the heart scarcely audible, the respiration slow and profound. In eight minutes the pulsations of the heart became distinct, and the respiration was hurried and difficult. In four minutes more sensibility returned to the anterior part of the body, and the animal moved its forelegs; the posterior extremities remained motionless and insensible. The pupils were excessively dilated, and the eyes glared hideously. Sight and hearing were, however, restored, for the dog watched my movements, and was startled by a sudden or loud noise. At this period the body was cold; in a short time the sensibility of the forelegs was again lost, the eye became fixed and glazed, the motions of the heart were feeble and quivering, and a rattling in the throat announced the period of dissolution. A little diluted spirits was now poured down its throat, which seemed to operate as by enchantment. In a few seconds the breathing became free, the motions of the heart accelerated, the energies of the system were revived, and, as if invested with new life and vigor, the animal in a minute or two was upon its legs, followed me when called, but whined piteously from the wounds on its surface, of which it was now sensible. The forelegs were moved with perfect freedom; the hind ones were not fairly lifted, but dragged along. It thus continued for about a quarter of an hour, when paralysis again returned, and, increasing progressively, terminated the function of animal life in exactly one hour and thirty-five minutes from the first injection.

He concludes, from a series of well and carefully conducted experiments, that ergot in large toxic doses affects chiefly the brain and the spinal cord; that both may be influenced together, or the spinal cord be attacked first; that in a concentrated form ergot paralyzes the system instantly, no resistance to its effect being discernible; milder preparations cause for a time great excitement, the nervous energy is roused, but sinks eventually under the influence of the poison; a much diluted solution, on the contrary, produces at first no apparent effect, but seems by a very progressive sedative action to deprive the system of its energy and so to exhaust it of life.

In *man* we see usually only the moderate forms of acute poisoning, and, as a rule, in pregnant women, the victims of criminal practice. By reason of idiosyncrasy, even ordinary therapeutic doses may show the same marked toxic action. In severe cases we observe a train of symptoms resembling in its essential points acute ergotism in animals, only in a milder degree. The patient is attacked by nausea, retching, eructations, vomiting, colic, and diarrhoea. Salivation is present, as a rule. The pupils are usually dilated, but may be contracted. Severe headache and giddiness ensue, and the sight is impaired. The patient manifests dejection and weariness, and complains of great muscular exhaustion. The pulse is weak, slow, and irregular; the arteries are relaxed and easily compressed; the skin is livid, indicating venous congestion. The respiratory movements are less frequent, with dyspnoea, and the temperature, as a rule, falls below the normal. In some cases severe neuralgic pains may be present. Drowsiness merges into stupor, the patient dying comatose.

Post-mortem examinations reveal, in animals, highly-marked venous engorgement, especially in the abdomen and cranium; the alimentary canal exhibits the signs of irritation; the bladder is generally distended, but may be well contracted. Autopsies in man are rare, and, as the cases are complicated with other conditions, there is little to be learned from the reports.

Chronic ergotism in animals assumes a form somewhat different from that of man. Wright, feeding dogs on food mixed with ergot, noticed them grow duller from day to day; they were thirsty, the

appetite became impaired, and the digestion disturbed. They lost flesh; acrid tears destroyed the hair on the face; the sight and hearing failed, paralysis of motion and sensation making its appearance pretty early, being more marked in the legs. In some cases hyperæsthesia could be observed. The pulse became feeble and slow; the breath was foetid, and the breathing was difficult; the stools and urine passed involuntarily; the temperature was reduced; and the animals died from exhaustion and paralysis in the sixth or seventh week.

On post-mortem, the muscles were found flabby and pale; the heart was full of dark blood; the bronchial and intestinal mucous membranes were injected and inflamed. The lungs of some of the animals contained tubercles, and some of the joints purulent collections.

Tessier, feeding pigs on ergotized food, observed the same effects as Wright; but he mentions also the occurrence of gangrene, which never took place in Wright's experiments.

Bonjean, Gross, and others fed fowls in like manner. The combs and wattles grew bluish-black, cold, hard, and brittle, and frequently ulcerated. Black blood flowed from the nostrils, and the plumage was shed.

Chronic ergotism in man presents itself either as raphania, "Kriebelkrankheit," spasmodic ergotism, or as gangrenous ergotism. Although the first has been observed mainly in Germany and Russia, and the second in France, we can not explain the differences of the toxic manifestations by the difference in the source of the poison. It is true that a number of French epidemics were induced by maize ergot, but we know that its action is identical with that of rye ergot. If we compare the symptoms of all three varieties of ergot disease, we shall notice a certain relationship between them. In the acute form we find exclusively grave nervous manifestations of a paralytic nature. These nervous disorders hold a very unimportant place in gangrenous ergotism, nutritive lesions being its prominent feature. Spasmodic ergotism occupies a middle ground. We find here certain nervous symptoms, paretic as well as irritative, but of a milder type than those of the acute form, and also nu-

trifling disorder, never reaching the intensity that it does in gangrenous ergotism.

It would appear, then, as if these three forms of the disease represented three different degrees of ergotic intoxication. This becomes still more evident if we compare the clinical course of the spasmodic and gangrenous varieties. The first supervenes earlier after the exposure, its course is more rapid, and death results from it sooner than in gangrenous ergotism. On the other hand, its symptoms resemble to some extent those of the mild acute poisoning, and may justly be considered as those of a subacute form of ergotism. In Germany and Russia, where the peasantry are poor and ergotic disease of the rye is more common, we naturally find a severer form of poisoning than in France, where the hygienic conditions are more favorable. Orfila * states that gangrenous ergotism is more apt to occur under prolonged exposure to the action of ergot.

SPASMODIC ERGOTISM. †—The first symptoms of the disease show themselves usually in a few days after exposure, and this may occur as early as the fourth day. It begins with a peculiar feeling of tingling and formication in the tips of the fingers and toes; and this may extend over the whole body. This is the first symptom to appear and the last one to pass away. The formication may increase, and there may be even actual anæsthesia. Vomiting and diarrhoea, with severe colicky pains, soon set in. A peculiar feature of the disease is intense hunger, which is probably a symptom of irritation of the gastric mucous membrane. Then comes on a feeling of discomfort, anxiety, and weariness, and of giddiness and unrest. The patient complains of distressing oppression in the epigastrium, severe headache, usually frontal, vertigo, noises in the ears, stupor following dizziness, and at times insomnia. The limbs may be stiff, and, as the result of the reflex centers of the spinal cord being affected, convulsive contractions of various groups of muscles may occur, frequently excited by the slightest touch, or apparently involuntary in character. They may pass into continuous contractions,

* Orfila, "Toxicology," translated by J. Nancrede, Phila., 1817, p. 351.

† Von Ziemssen's "Cyclopædia," xvii, p. 904.

which particularly affect the flexors. These cramps may last a variable length of time, are very painful, and are followed by a state of utter exhaustion. The convulsions may be very extensive, tetanus and epilepsy may occur, and even cataleptic conditions have been observed. In animals one-sided rotatory movements have been seen. As the disease advances, the convulsions become more frequent and general, but, sooner or later, paralytic phenomena occur in the sphere of motion, sensation, and reflex movements. The pupils are contracted or distorted, the eyes are fixed, the skin is bathed in cold perspiration, the urine is suppressed or only retained by the spasms of the vesical sphincter. The pulse is slow, weak, and irregular. In severe cases the patient loses the power of sight, hearing, and speech. He may become unconscious or delirious. At this stage the face is pale and sallow, the surface of the body is cold, and, as the convulsions occur, with increasing paralysis of the heart, the disease is closed by death, which may occur as early as the third day. The occurrence of blindness may be preceded by various visual disturbances—colored and doubled vision, photophobia, hemiopia, periodic amblyopia, and hallucinations. The latter in the sphere of other senses are not uncommon.

This train of symptoms would place spasmodic ergotism in an intimate relation to the acute poisoning; the difference is accounted for by the fact that the system is not entirely overpowered, and the opportunity is afforded for the development of those specific nervous disorders which are peculiar to this substance. But, as the disease may last sometimes from one to two months, and very seldom lasts less than two weeks, we may observe in some cases also trophic disorders. About two weeks after the beginning of the disease pustules and even furuncles may appear, the fingers may be attacked by whitlows, and the nails may be diseased toward the close of the month. It is not very uncommon to meet with gangrenous processes in different parts of the body. Should the patient recover, the nervous symptoms gradually subside, and, after a protracted convalescence, a complete recovery may take place; but at times permanent lesions may remain—stiffness of the joints, paralysis, muscular weakness, tremor, epilepsy, imbecility, optic disorders,

etc. The post-mortem appearances are the same as in the acute and chronic poisoning of animals.

GANGRENOUS ERGOTISM.—In the beginning of the disease we find some of the symptoms of the spasmodic form, but they are less severe and not so marked. We may have violent cutaneous irritation and other disorders of the sensitive nerves. Symptoms referable to the cerebral nervous system are met with also—headache, dizziness, occasional contractions of the flexors, and disturbances in the sphere of the organs of special sense. Retching, nausea, vomiting, and diarrhoea appear early in the disease. But the specific symptoms of gangrenous ergotism, although they may make their appearance in a few days, do not usually show themselves until two or three weeks later. The part to be affected grows cold, and the feeling of cold may be intense; then erysipelatous redness spreads over it. The epidermis is soon raised by serous exudation; after the latter has escaped, the denuded surface appears gangrenous, and dry gangrene rapidly develops. During the first part of this process there is a good deal of pain, but later on the part becomes insensible. As a rule, the gangrene is dry, but in some cases the moist variety may be seen. The parts that are usually affected are the toes and the feet, less frequently the fingers and hands, in some cases the nose and the ears. As a rule, the gangrenous process is limited, but in some cases it may extend to the trunk. Cases are on record in which all four extremities were attacked and destroyed. We have to expect a severe drain on the system, and the condition is aggravated by the absorption of the poisonous matter. In the course of the disease the patient suffers from a low continued fever; phthisical symptoms may develop. Death results from exhaustion, pyæmia, or septicæmia. If the gangrenous process be not very extensive, the patient may recover; otherwise the prognosis is unfavorable. The disease may last several months.

Autopsies do not reveal anything different from what is to be expected under the circumstances. Barrier asserted that the arteries leading to the gangrenous region were diseased, but Bonjean and others have found them normal.

Treatment of Ergotism.—In all cases further introduction of

ergot into the system should be arrested, and that which is already in the alimentary canal should be removed as speedily as possible. Griepenkerl recommends the use of tannic acid, but it can be of benefit only if ergot is present in the stomach and intestines. Cardiac and nervous depression should be treated by stimulants. Alcohol exerts a very beneficial action even when there are grave paralytic symptoms of acute ergotism. Spasms and muscular pains must be treated by anodynes, electricity (central and local electrization), warm baths, and friction. Von Boeck recommends, properly, the use of nitrite of amyl to relieve the spasms of the arterial system. A supporting and stimulating regimen will meet the remaining indications. A perfect drainage of the ichorous discharges should be established in conjunction with the usual antiseptic dressings. Blood poisoning, if present, is to be treated as under other circumstances.

ACTION OF ERGOT ON TISSUES, ORGANS, AND FUNCTIONS.—In the preceding pages we have made ourselves familiar with the general aspect of the action of ergot on the system. All the essential features of its physiological action have been referred to, and it remains now to examine each in detail to complete this part of our subject.

Action of Ergot on the Nervous Tissue.—From the description of the ergotic intoxication, it is evident that the nervous system is profoundly affected by ergot. We must determine how it manifests itself, and what parts of the nervous system are acted upon by the drug.

a. Nervous Centers.—There can be no doubt that their function is very seriously influenced by ergot. In fact, the greatest part of the symptoms of ergotism is due either to their paralysis or to their irritation, with subsequent paralysis. It is important to decide if these symptoms are due to the direct action of ergot on the nerve cells or to the primary disturbance of the circulation within the cranium and the vertebral column. That the latter plays a very important rôle in the evolution of ergotic symptoms, there can be no doubt. We find in the experimental pathology and pathology of nervous diseases many facts demonstrating the great dependence

of the ganglionic functions on their blood supply. But to follow the example of Stillé and Maisch * by ascribing all the nervous disturbances caused by ergot to the altered circulation would be to commit a grave error. The fact itself that the circulation is influenced by ergot speaks in favor of its direct action on the nerve centers (vaso-motor ganglia), and there is no reason why we should doubt the possibility of other centers being also similarly affected. It is true that the task of discriminating as to the immediate cause of a great many ergotic symptoms, if taken separately, is almost impossible. Still we can not admit that such a train of symptoms as is observed during the rapidly fatal cases of acute ergotism can be caused alone by the interference with the circulation. Outside of ergotism, simple anæmia or vascular relaxation can cause headache, dizziness, drowsiness, stupor, delirium, mania, various functional disturbances in the sphere of sight and hearing, nausea, vomiting, paræsthesia, various motor disturbances, etc. And in the case under consideration we may ascribe them to the same cause. But these symptoms are far from exhausting all that is seen in poisoning by ergot, and, what is more, it is safe to assume that the above-enumerated symptoms are intensified by the direct action of ergot on the nerve cells involved in their manifestations.

On the other hand, there is a group of symptoms which can not be so readily connected, if at all, with the changes in the blood supply. Here belong those referable to the motor centers of the spinal cord, the cerebral and peripheral vaso-motor ganglia, the cardiac centers, the motor (contracting) centers of the iris, etc. Various trophic disturbances (ulcers, gangrene, etc.) are also most likely due to the trophic centers being affected by ergot. As to the motor centers of the uterus, bladder, intestines, etc., the evidence is decidedly in favor of the direct action of ergot. This will be discussed more fully under the appropriate heads; it will suffice at present to conclude that ergot acts upon the nerve cells directly, in which it is assisted by the circulatory disorders. This action manifests itself as an irritation, or as an irritation with subsequent paralysis, and, when the quantity of the drug is great, as immediate

* Stillé and Maisch, "National Dispensatory," Phila., 1879, p. 536.

paralysis. It is clear that ergot acts on all the nerve centers irrespective of their functions, but the motor centers of the inorganic muscular tissue appear to be influenced in a particularly prominent manner.

b. Nerve Fibers.—In deciding upon the mode of action of ergot on the nerves it is important to eliminate its influence on the cerebro-spinal centers. This can be accomplished by bringing the nerves into immediate contact with some fluid preparation of ergot, and otherwise excluding the influence of the centers. According to Köhler,* ergot diminishes the irritability of the *sensitive nerves*. Nikitine, who experimented with sclerotic acid, finds that the peripheral ends of the sensitive nerves are paralyzed by it. Köhler states that the *motor nerves* are similarly affected by Bonjean's extract, while Wiggers's ergotine produces the opposite effect. Nikitine did not notice any effect on the motor nerves from the use of sclerotic acid, and Haudelin† does not think that the nerves are affected by ergot at all, the symptoms being due to the central influences. It is evident from the foregoing that the action of ergot on the nerve fibers is not a very pronounced one, playing, in fact, a subordinate rôle.

Action of Ergot on the Muscular Tissue.—The two varieties of muscular tissue, voluntary and organic, differ from each other in many respects, the essential difference consisting in their respective modes of innervation. The skeleton muscles are under the immediate control of the cerebral volitional centers. Their spontaneous activity is due to the spinal reflex centers, whose function is regulated by Setschenoff's inhibitory centers lodged in the medulla oblongata. So that the motor impulses are derived exclusively from the cerebro-spinal axis, with which the muscles are connected only by the conductors of the impulses. The organic muscular tissue is to a great extent under the control of the motor centers lodged within itself or in its immediate vicinity; the function of these centers is regulated by the centers located in the cerebro-spinal axis, which are not within the reach of volition. As to the muscular substance itself, although it differs in both cases materially from

* Virchow's "Archiv," lx, p. 384.

† *Op. cit.*

the standpoint of anatomy, physiologically the difference is slight and immaterial.

We must ascribe, then, the dissimilarity in the behavior of the two kinds of muscular tissue under the influence of ergot rather to the difference in their respective modes of innervation than to that of their structure. In fact, there is not the slightest evidence that ergot has any action whatever on the muscular tissue itself. This is very easily verified on the skeleton muscles. The motor paralysis does not appear until the stage of general paralysis is reached, while the preceding motor disturbances (convulsions, spasms, tremors, etc.) are due to the action of ergot on the spinal motor centers. In this all observers unanimously agree. Köhler, who studied this question very thoroughly, states that the type of the muscular contractions, as shown by Helmholtz's myographion, is not altered by ergot in the least; that the electro-contractility is not changed, and is the same before and after death. Nikitine also arrived at the same conclusions. Similar investigations with regard to the organic tissue are much more difficult on account of the intimate connection existing between the motor centers and the muscular tissue. This subject will be treated of more extensively when speaking of the action of ergot on the different organs composed of organic muscular tissue; we may say here that it is more consistent with the result of experiments to draw the same conclusion as in the case of the voluntary muscular system. In some cases there can not be the least doubt as to its correctness, and where the evidence is not so pointed there will be no reason not to adopt a uniform view.

Ergot has no effect whatever upon the remaining tissues. The glandular organs are acted upon by it through the medium of the nervous system and the circulation.

From the preceding pages we may conclude, then, that the *entire physiological action of ergot is based upon its action on the nerve cells in general, and on certain motor centers in particular, consisting in irritation, resulting in their paralysis if the quantity of the substance is great.*

ACTION OF ERGOT ON THE HEART.—We know that ergot produces

a decided effect on this organ, and this was noticed by the earliest observers. The pulse in acute ergotism may be at first accelerated, to be retarded toward the close. During chronic ergotism the pulse is always slow, and the same effect is produced when a moderate quantity of ergot is introduced into the system. According to Nikitine, sclerotic acid acts in this manner only on frogs; in the warm-blooded animals even large doses failed to produce this effect. Haudelin observed, first, acceleration of the pulse with subsequent retardation. Eberty,* by injecting 0.1 gramme of ergotine into the gastric vein of a frog, reduced the pulsations from 30 to 6 a minute, and the second dose arrested the heart-beats completely. But in warm-blooded animals the pulse rate seldom falls below 60, although Hooker† reported an experiment on a medical student, who took two drachms and a half of oil of ergot with the effect of diminishing the frequency of the pulse from 82 to 36. According to Gibbon,‡ the maximum effect is usually observed in a half-hour after the exhibition of ergot, and the effect may last, according to Hooker, for a number of days. The reduction of the pulse rate is always greater if the heart's action is excessive, and the sedative influence of ergot on the circulation is to be seen under the most favorable conditions during a febrile state.

Not only the frequency of the pulse is affected, but the heart's contractions also become weak and irregular. Should a toxic dose be given, the heart stops in diastole; and then no stimulant—mechanical, electrical, or chemical—can make the organ respond. Ergot acts mainly on the ventricles; the auricles apparently escape almost entirely. Rossbach* and Wernich state that if the heart be carefully watched it is noticed that the ventricles contract once to every two contractions of the auricles, and that the latter do not show any change from the normal type, while the ventricular diastole is incomplete, and the contraction of the separate fibers is not simultaneous, but alternating, giving the appearance of peristalsis

* Virchow and Hirsch, "Jahresbericht," 1873.

† Stillé, "Therapeutics and Materia Medica," ii, p. 585.

‡ "Am. Jour. of the Med. Sci.," Jan., 1844.

* Virchow and Hirsch, "Jahresbericht," 1874.

and also as if certain fibers were persistently contracted while other, were relaxed.

There is some evidence that ergot exerts on the heart the same effect as on the other organs composed of organic muscular tissue, namely, reducing its size by contracting and condensing its fibers. Of course, this effect can not be very marked in a state of health any more than in other cases, but, when there exists an unnatural relation of the organ, its action is prompt and decided. Willebrand * noticed the diminution of the healthy organ. The same effect was also observed in frogs. This subject will be more fully treated when we speak of the use of ergot in cardiac affections.

It remains now to make an effort at determining in what manner ergot produces these effects on the heart. They can not be due to ergot paralyzing the cardiac muscle, as all the earliest observers thought, and as Rossbach has more recently affirmed. If we give ergot to an animal which is completely atropinized, we find that it fails to affect the heart even when used in very large doses. From this we infer that between these two drugs there exists a very striking antagonism in their action on the heart. Atropine, as the reader knows, paralyzes the cardiac inhibitory centers, which we conclude from the acceleration of the pulse, and from the facts that in the atropinized animal both section and irritation of the pneumogastric nerves fail to produce their usual effects. Ergot, on the other hand, retards the pulse, and when the cardiac inhibitory centers are paralyzed by atropine it fails to act, showing that it acts on the heart by stimulating these centers. When it induces the arrest of the heart, this occurs in the diastole, the organ being relaxed and flabby—a picture identical with that of the arrest of the heart by a strong irritation of the cardiac inhibitory centers through the medium of the pneumogastric nerves. That ergot acts on these centers directly, and not on the medullary centers of the vagi, we conclude from the fact that ergot produces also the same effect on the heart after they have been destroyed. Such a decided action of ergot on one part of the cardiac innervation suggests, naturally, the thought of the probability of other parts of it being

* Dybkowsky, *ibid.*, p. 612.

affected by it also. This is not apparent in the usual experiments on animals, but clinical evidence speaks in favor of ergot acting on the cardiac excito-motor centers as a stimulant. Eberty, Boreidscha,* Köhler, and others think that ergot affects the cardiac centers directly, while Wernich is inclined to ascribe the results to their irritation by the diminished blood-supply of the organ.

Action of Ergot on the Blood-vessels.—Some modern observers deny entirely any active contraction of the arteries resulting from the use of ergot. Boreidscha is led by the results of his experiments to the conclusion that there exists a marked similarity between the action of ergot and that of nitrite of amyl on the vaso-motor centers. The difference, according to him, consists in ergot acting mainly on the splanchnic nerves, while nitrite of amyl acts chiefly on the cervical sympathetic. He asserts that ergot can produce a further lowering of the blood pressure after nitrite of amyl has accomplished its full effect. The arrest of hæmorrhage with ergot is explained as a secondary result of the diminution of the heart's action and of the lowered blood pressure, permitting the elasticity of the blood-vessels to have full play. Zweifel† explains the contraction of the capillaries in cases of hypodermic injection or local application of ergot as a simple reflex phenomenon due to the action of an irritating and painful agent, as similar results follow the use of a great many irritating substances, having no direct relation to the circulation. If the animal be narcotized, and consequently the painful reflexes abolished, he states that the use of ergot fails to induce the contractions of the blood-vessels. Should this occur, the effect is but slightly marked and of brief duration, being rapidly followed by the dilatation.

These are the only observers who do not share the generally accepted opinion that ergot produces an active contraction of the vessels. The idea itself is a very old one. Courhant, as early as 1827, advanced this theory. It was adopted by Sée in 1842, and supported by Sovet in 1848. Later on Klebs‡ proved experimentally that ergot produced anæmia and a rise of blood pressure. And,

* "Moskow. Pharmakol. Rabot.," 1876, p. 50.

† *Op. cit.*

‡ Virchow's "Archiv," xxxii, p. 490.

although this view was fully established by clinical experience, not until 1869 was the contraction of blood-vessels actually observed under the microscope, by Briesemann.* This was confirmed by Holmes† in 1871, who drew with the camera lucida the appearances of the blood-vessels before and after the exhibition of ergot, and also by all subsequent investigators—Patel,‡ Wernich, Niccol and Missop,§ Eberty, Brown-Séquard,|| Kersh,^ Köhler, Peton,◇ and others. But the actual mode of production of this contraction of the blood-vessels is more difficult to demonstrate. The same question arises here also, Is it due to the action of ergot on the vaso-motor centers (cerebro-spinal and peripheral), or is it due to the direct action of ergot on the contractile cells of the blood-vessels? The cerebro-spinal influence is placed beyond doubt. All observers agree on this point. There is also sufficient evidence of the fact that ergot acts on the blood-vessels when the part is separated entirely from the cerebro-spinal axis and the sympathetic system. Holmes observed contraction of the blood-vessels after he had severed all their vaso-motor nerves. Peton noticed an immediate effect when ergot was injected into the observed part, but if all the nerves leading to it were cut, and the injection made at a distant point, the contraction occurred also, but was delayed. Wernich and Köhler are also in favor of the peripheral action of ergot.

Testimony to the opposite is not wanting. Voigt,‡ Wood,‡ and Eberty failed to see the vascular contractions after the separation of the vaso-motor nerves; they admit them to be possible only on condition of intact vaso-motor nerves. Independent of the experimental evidence in favor of the peripheral action of ergot, we have also abundant clinical facts to the same effect. Local applications of ergot contract the blood-vessels, and this occurs when ergot is used in quantities making it impossible to advance the idea of its action through absorption, and so dilute as to exclude the idea

* Inaug. Diss., 1870.

† "Arch. de Physiol.," etc., 1870, p. 384.

‡ Inaug. Diss., 1871.

* "Brit. and Foreign Med.-Chir. Rev.," I, p. 200.

|| "Arch. de Physiol.," 1870, p. 484.

^ "Memorabilien," v, p. 200.

◇ Thèse de Paris, 1878.

‡ "Berl. klin. Woch.," 1869, No. 12.

‡ "Phila. Med. Times," 1874, p. 519.

of a reflex effect from irritation. With regard to the action of ergot on the veins, Wernich observed them dilate, while Patel and Köhler state that they are acted upon by ergot in the same manner as capillaries and arteries. This effect on the blood-vessels occurs only if the quantity of ergot is not great; if, on the contrary, the dose is toxic, instead of the contraction we have a complete paralysis, giving rise to the venous congestion so constantly seen in animals and men poisoned with ergot.

As in the case of the heart, we are led to conclude that ergot acts on the blood-vessels through their nerve supply, and not upon their muscular structure. The greatest effect is due to the irritation of the vaso-motor centers in the medulla oblongata and the spinal cord. The peripheral action is readily explained by the existence of a rich ganglionic network in and about the blood-vessels, which is acted upon by ergot in the same manner as the medullary vaso-motor centers.

Action of Ergot on the Blood Pressure.—The state of the blood pressure is determined by the conjoined action of the cardiac contractions and the lumen of the blood-vessels. The greater or less is the vigor of the cardiac action, the greater or smaller is the caliber of the blood-vessels, the greater or less will be the blood pressure. But ergot acts in the two opposite directions—by reducing the energy of the heart it tends to lower the arterial tension; on the other hand, by contracting the blood-vessels it will operate in the contrary manner. In large toxic doses, by paralyzing the heart and the vascular tonus, it will effect a marked fall of the blood pressure. It is evident, then, that we can not expect to obtain uniform results with regard to the vascular tension, as they differ not only according to the amount of ergot used, but also according to the peculiar conditions of the circulatory organs present. Drasche,* using the therapeutic doses on healthy men, obtained a rise of the blood pressure, a conclusion based upon the study of the characters of the pulse and of the sphygmographic tracings. Holmes, Klebs, Ebert, Köhler, and others observed in animals an increase of the tension; and Handelin, Hermann, Wernich, and

* "Wien. med. Woch.," 1872, 38, 40.

Boreidscha arrived at the opposite conclusion. These contradictory statements are such only in appearance, as they relate to the different stages of the physiological action of ergot on the circulation. The first effect of ergot is to increase the blood pressure, but if the quantity of ergot used be excessive, the period of the increased tension may be very brief, and even be entirely wanting, on account of the rapidly developing vascular paralysis. If a moderate or small amount of ergot be introduced, the period of increased tension will be more marked, and the secondary reaction may be absent. In man the circulatory apparatus may present conditions in which even ordinary therapeutic doses will produce a well-defined sedative effect on the circulation entirely disconnected from the paralysis of the heart or of the vaso-motor centers. This occurs if ergot is given to persons whose heart is in an abnormal state of activity, as in fevers, inflammations, cardiac hypertrophy, palpitation, etc. I will refer the reader to the description of the action of ergot in aneurisms, where the sedative action of ergot on blood pressure is particularly well marked.

Action of Ergot on the Organs composed of the Organic Muscular Tissue.—The stomach, intestines, uterus, and bladder are identical in their structure and mode of innervation with the heart and the blood-vessels, and consequently we should expect to find the same effects on them from ergot.

Intestines.—Wright, on opening the peritoneal cavity of animals poisoned by ergot, observed an active peristalsis. A similar effect was noticed by Wernich on animals during life and with the peritoneal covering intact. Haudelin and Peton observed the same. According to Nikitine, sclerotic acid always produces an active peristalsis in warm-blooded animals. Diarrhœa is a very common symptom in patients suffering from chronic ergotism (it was present in seventy per cent. of patients during the epidemic described by Swjatlowsky), while vomiting is of less frequent occurrence. This would justify us in the belief that we have to deal in these cases with diarrhœa produced not only by the irritation of the intestinal mucous membrane, but also, at least in part, by the action of ergot on the motor centers of the intestinal muscular tissue. At times,

on the contrary, the patients suffer from constipation, apparently due to the tonic spasm of the coats of the intestines. Unfortunately, we possess no facts to determine the exact mode of action of ergot on the innervation of the intestines. I have failed to find any experiments relating to the action of ergot on the stomach.

Bladder.—In animals poisoned with ergot, the bladder may be found distended with the urine, or empty and firmly contracted. In the first instance we have a spasmodic contraction of the vesical sphincter in the foreground, while in the latter the entire muscular structure of the organ is under the influence of ergot. The experiments of Peton are more thorough than those of any other observer. He noticed soon after an injection of ergot the appearance of fibrillary contractions resulting in the complete evacuation of the organ; in other cases the contractions alone were seen. Wernich observed the same phenomena, and he recommends close attention to the regularity of micturition in patients treated with ergot, and, should retention occur, the use of the catheter.

Uterus.—The action of ergot on the uterus constituted at one time the most prominent feature in the entire range of our knowledge of its physiological properties. That ergot can induce contraction of the pregnant uterus, resulting in the expulsion of its contents, is well known. The same effect is produced also on animals fed on food mixed with ergot. It is also well established that the ergotic uterine contractions differ materially from the normal parturient type, being of longer duration, assuming the character of a spasm, and frequently manifesting themselves chiefly at the lower segment of the uterus. It is also a well-known fact that the energy of the action of ergot is in proportion to the length of time the gestation has existed, and that it is the most intense during labor. That the uterine contractions thus induced may be very powerful we have abundant proofs. There are well-authenticated cases of various traumatic accidents to the organ and the foetus, such as laceration of the uterus, crushing of the child's head,* and other injuries. More interesting are the action of ergot on the non-pregnant organ and the manner in which it is produced. The experiments of Wer-

* Veit, "Ztschr. f. Geburtsh. u. Gynäk.," iii, 2.

nich show that ergot induced fibrillary contractions of the muscular tissue of the uterus, and this was also noticed by Schlesinger. Nikitine found that sclerotic acid induced them in the normal organ, and that if they were present they were intensified by it. But the disputed question is, the manner of their production. According to Schlesinger and Oser,* who discovered the existence of the uterine motor centers in the cerebro-spinal axis, the uterine contractions are due to anæmic irritation of these centers; but Wernich believes they are due to the direct action of ergot on these centers, because the contractions occur some time after the appearance of the cerebro-spinal anæmia. He states also that, if the spinal cord be cut in the lumbar region, ergot fails to act on the uterus, and from this fact he concludes that the motor impulse is of cerebral and not of peripheral origin. The more recent observations of Boreidscha question the correctness of the latter statement. He noticed well-marked contractions of the uterus after all its nervous connections with the cerebro-spinal axis had been severed, showing that, at least in part, they were due to ergot acting on the motor centers within the uterine structure, the existence of which is admitted by all. The behavior of the uterus under ergot is, then, identical with that of the blood-vessels. The maximum effect in both cases is due to irritation of the cerebro-spinal centers, but it is possible also to demonstrate an active participation of the interstitial motor centers.

Action of Ergot on the Iris.—Alterations of the pupil belong to the most constant symptoms of ergotism. In acute poisoning, where we witness paralytic manifestations, the pupils are dilated. During the early stages of spasmodic ergotism, characterized by the irritative action of the drug, the pupils are contracted in a very marked degree. But toward the close of the chronic poisoning, with the appearance of the paretic and paralytic symptoms, the pupils present an uneven aspect, and at death they are dilated. The action of ergot on the iris resembles, then, very much that of the Calabar bean. According to Comperant and McEvers,† ergot may even counteract the effect of belladonna. In the absence of

* "Med. Jahrb.," 1872, 1873, 1874.

† "Bull. Gén. de Thérap.," xxxvi, 1848, p. 41.

special investigations to determine the *modus operandi*, we must be satisfied with the conclusion that ergot excites at first the motor apparatus of the orbicular fibers of the iris and paralyzes it in toxic doses.

Action of Ergot on the Glands.—The activity of the glands is controlled by two kinds of nerves—vaso-motor and glandular proper. The first regulate the energy of the circulation in the blood-vessels surrounding the follicles and acini, the latter terminate in the glandular epithelium, and influence their nutritive processes, hastening or retarding the disintegration of the secreting cells, the secretion being the diluted product of this cellular dissolution. The action of ergot on secretion is very slight in health, and frequently not noticeable at all. We must turn our attention to the bedside for the purpose of estimating this point in the physiological properties of ergot. Its power of arresting or diminishing all kinds of hypersecretion is very marked, and if we bear in mind that in health its action in this respect is very slight or *nil*, and that the hypersecretion occurring in man as a morbid condition, or produced artificially in animals by irritating the vaso-dilating nerves, is chiefly an exaggerated transudation, and not the normal secretion increased in quantity, we may readily conclude that ergot, in diminishing the excessive flow of a secretion, accomplishes this result by inducing anæmia of the glands, and not by affecting the secretory nerves. Still the latter may be acted upon also, only we have no means of ascertaining the fact. The function of the nerves is very easily suppressed or excited; minute doses of atropine, pilocarpine, opium, and some other substances readily depress or exaggerate the energy of the glands. The first-named substances act on the glandular nerves, but we are ignorant as to the mode of action of others, like sulphuric acid, oxide of zinc, preparations of lead, tannic acid, etc. Ergot, being a very decided nervine, may also act on the glandular innervation, and, if this is the case, the action is most likely of a sedative, paralyzing nature.

All observers agree that ergot induces profuse *salivation*. The cause of this lies partly in its acrid taste, and partly in the irritation of the alimentary canal. *Digestion* is invariably disordered if ergot

is used for a long time, in consequence of gastro-enteritis and circulatory disturbances in the adjacent glands diminishing the secretion of the digestive fluids. Haudelin did not find any material change in *lachrymation* or *defecation* in the animals experimented upon in the usual manner. The secretion of *urine* is not affected by ergot in a sensible manner (Haudelin, Drasche, Peton, and others), but these experiments are rather difficult to carry on, on account of the disturbances in the function of the bladder. *Perspiration* and the secretion of *milk* are not affected by ergot in a state of health to any appreciable extent, but all these three secretions are materially modified if morbidly increased. The same is applicable also to the *mucous* secretions. We have no positive data with regard to the secretions of the *liver*, the *pancreas*, and the remaining glands. The *spleen* is diminished in size, but the effect is not marked on the healthy organ. Ergot may at times cause *seminal emissions* by irritating the sexual centers of the lumbar spine.

Action of Ergot on the Temperature.—In nearly all accounts of epidemics of ergotism, coldness of the skin and a feeling of cold are mentioned as prominent features. In the recent epidemics of ergotism in Russia, described by Swjatlowsky, he noticed elevated as well as lowered temperature. Out of thirty-five cases, nineteen of which were severe, in only three patients did he observe the axillary temperature below the normal (95.6° F.), but the elevated temperature did not exceed 99.8° . According to Drasche, the therapeutic doses in healthy man produce a slight rise of temperature— 0.1° . Large toxic doses always depress the temperature in a very striking manner. In this agree Köhler, Galippe and Baudin,* Nikitine, Kersh, and others. But of course the proper field to study the antipyretic properties of ergot is at the bedside, and we have some evidence that it possesses them to a marked extent. Still, this is yet an unexplored field. Hayem† found ergot to exert a more decided control over the temperature of typhoid fever than quinine or digitalis. Gillette‡ speaks highly of the action of ergot in rheumatic fever.

* "Gaz. Méd. de Paris," 1878, p. 150.

† "Am. Jour. of the Med. Sci.," 1876, i, p. 56.

‡ "Rev. de Thérap. Méd.-Chir.," 1874, p. 455.

The reader will see that in croupous pneumonia also ergot tends to lower the temperature. The same effect is noticed also in sunstroke, etc. But the rise of temperature may be due to so great a variety of causes that the propriety of using the term antipyretic seems questionable, except in connection with hydrotherapeutics.

Action of Ergot on Respiration.—Dyspnœa is a very common symptom of ergotism. Swjatlowsky noticed in all cases reduced frequency of respiration (14–16), and this was more marked in children. Experiments on animals give the same result, and Nikitine lays particular stress on the depressing action of ergot on respiration. According to him, toxic doses of ergot stop the respiration previous to the arrest of the heart's action, so that death is due to asphyxia and not to cardiac paralysis. Previous to the arrest of the respiratory movements they may be very much accelerated. Drasche did not notice any effect from therapeutic doses. Dyspnœa, if it is due to the action of ergot on the nervous system, must be ascribed either to irritation of the laryngeal branches, or to paresis of the pulmonary branches of the pneumogastric nerves.

Action of Ergot on Nutrition.—We do not possess any facts relating to the influence of ergot on nutritive exchange (*Stoffwechsel*). From our knowledge of the physiological properties of ergot, we may infer that it can not be great. Ergot differs in this respect from iron, alkalies, and other substances having a direct bearing on the chemistry of the system. The grave nutritive lesions peculiar to chronic ergotism are caused by its action on the trophic centers of the spinal cord. It would be out of place to review the disputed question of the existence of these centers. It will suffice to say that the negative assertion is based upon experiments in physiological laboratories, the least competent method of approaching the subject, as we have no means of reaching, modifying, or suspending the function of these centers in a direct manner without producing at the same time grave complications, entirely obscuring the operation of the forces in question. The method of severing the nervous connections of a part from its nerve centers is open to the same objections; and, what is more, entirely different conditions are created, because in disease the nervous connections are intact; only the function of the centers

is modified. Those who advocate the existence of trophic centers base their assertion on clinical observations, claiming properly that the single vaso-motor disturbances are not competent alone to produce the various local nutritive disturbances observed so frequently in the course of a great many diseases, or constituting the disease itself. The latter view is rapidly gaining favor with pathologists, and the drift of the present evidence is decidedly for the existence of centers having a direct control of local nutrition. It is yet premature to determine in what manner this function is exercised, or what are the anatomical characteristics of these centers; we know fully as little of a great many other topics having a legitimate place in science. Ergot attacks the nutritive centers of the skin in preference to others, but its action may have a much wider range—those of the joints, blood-vessels, internal viscera, etc., may also be affected. The ultimate result of this action is impaired vitality of the part, terminating in its destruction and gangrene, or in the occurrence of suppuration, low forms of inflammation, tubercle, etc. With regard to the general nutrition, it is apt to suffer from the prolonged use of ergot. This is caused partially by the disturbed state of the alimentary canal, and also by the injurious action of the drug on the nervous tissue.

EFFECTS OF ERGOT ON THE FŒTUS.—At present ergot is used very seldom in the early stages of labor, and opportunities of witnessing its ill effects on the child are rare. In former times this practice was very common, bringing opprobrium on the drug. Unquestionably it was the cause of a great many still-births, but it has been also held responsible for the unfavorable course of parturition when this was due to some other conditions. As has already been stated, the use of ergot was interdicted in France in 1774. It was readmitted at a later period; still, the indiscriminate and frequently injurious use of it induced the Prefect of the city of Paris to send to the Academy of Medicine in 1855 a communication, in which he called the attention of the faculty to the increasing rate of still-births, which he ascribed to ergot, and inquiring about the propriety of restricting by legal regulations the use of ergot in obstetric practice, if not entirely prohibiting it. During the discussion of this sub-

ject, St. Claire Deville * brought to light some very damaging facts if we admit them to be due to the use of ergot. He found that the rate of still-births in Paris in 1829 was only five per cent. of the entire number of births; in 1839 this figure rose to nine per cent., and in 1855 to eleven per cent. The child is affected by ergot in a number of ways. The placental circulation is interfered with; after the rupture of the membranes powerful and spasmodic contractions of the uterus compress the umbilical cord and prevent the free flow of blood through it; they may lead even to traumatic injuries to the child. If ergot is given early in labor, the normal type of uterine contractions is perverted, retarding the completion of the act, and jeopardizing the life of the child. These considerations refer only to the action of ergot on the child during parturition, and from the mechanical stand-point. The question, if ergot has any constitutional effect on the child when taken by the mother, is difficult to answer. Hardy † states that he has observed retardation of the foetal heart beats. It is well known that remedies pass from the mother to the child, and act on the latter in their peculiar manner.‡ There is no reason to think that the same does not occur with ergot. Still, it is established that ergotized mother's milk has no injurious effect on the child.

SYSTEMIC EFFECT OF THERAPEUTIC DOSES OF ERGOT.—Prolonged administration of ergot may affect the patient injuriously. First to suffer is the alimentary canal, when the drug is taken by the mouth. If introduced by hypodermic injection or by the rectum, the digestion is spared, and we must watch for the injurious results in the direction of the nervous system. In some patients a train of symptoms resembling a mild form of spasmodic ergotism is very rapidly developed; in others, the drug is borne still worse—something like an acute ergotism develops from a few small doses. In women we are apt to see very painful uterine colic. In other patients ergot may produce angina pectoris, retention of urine, etc. But, as a rule, patients bear ergot very well, and very little is no-

* "Lancet," June 13, 1859.

† Wood and Bache, "United States Dispensatory," Phila., 1875, p. 383.

‡ Kubassoff, "Inaug. Diss.," St. Petersburg, 1880

ticed beyond the action of the drug in regard to the special symptoms for which it was prescribed. We meet with reports of patients taking very large doses of ergot during a long period without suffering from it.* One of the most constant manifestations of therapeutic doses is its sedative action on the heart.

CONDITION OF ERGOT IN THE SYSTEM, AND ITS ELIMINATION.—Ergot is absorbed into the circulation unchanged, and acts on the system as such. We can not say if it suffers any changes subsequently, or in what form and by what channels it is eliminated. Only in one case, that of Neubert, the effort was made to discover its presence in the system. After the tissues had been treated with alcohol, and the latter evaporated, a substance was obtained closely resembling Wiggers's ergotine. Wright was able to extract from the blood of animals poisoned with large quantities of ergot an oily matter, becoming black on heating, and evolving the odor of an old tobacco-pipe, apparently oil of ergot. It is well established that ergot does not pass into the milk. I have found only a single instance in which ergot was discovered in the excretions. A woman suffering from a uterine fibroid tumor was placed on the use of ergot; in the discharge from the womb was discovered a substance answering to the usual test for ergot.†

RELATION OF ERGOT TO OTHER MEDICINAL AGENTS.—We may infer from the preceding pages that ergot occupies a very distinct place in the materia medica, although resembling a number of substances to a greater or less extent. On the other hand, it possesses properties entitling it to be regarded as a physiological antagonist to a group of agents. *Strychnine* acts on the system in a manner most nearly allied to that of ergot. Both act similarly upon the motor centers of the spinal cord, the cardiac inhibitory, the vasomotor, and all other motor centers of the organic muscular tissue. Therapeutically, it is simply a question of habit in some cases which of the two drugs shall be prescribed. But the main feature of strychnine is its action on the spinal motor centers of the voluntary muscular tissue, which are affected by ergot to a much lesser de-

* Drysdale, "New Remedies," 1876, p. 15.

† "Practitioner," 1879, p. 81.

gree. *Digitalis*, like ergot, acts on the cardiac inhibitory and motor centers and the other motor centers of the organic muscular tissue; it also depresses the temperature. But its predominant stimulating action on the heart distinguishes it essentially from ergot as a therapeutic agent. *Quinine* possesses also in a mild degree a stimulating action on the organic motor centers; in large doses it paralyzes the vaso-motor and cardiac centers; it depresses the temperature. *Calabar bean* resembles ergot in many respects. Both contract the pupil, irritate the cardiac inhibitory centers, retard the respiration, raise the arterial pressure, and increase the intestinal peristalsis. The main difference between them consists in an early occurrence of the paretic state of the voluntary motor apparatus, even after doses of the Calabar bean not entirely toxic. We may, then, form an arbitrary group of the excito-motors of the organic muscular tissue, the typical representative of which will unquestionably be ergot. As antagonists to ergot, nitrite of amyl and atropine may be mentioned. *Nitrite of amyl* paralyzes the walls of the blood-vessels, and acts as a depressor to the motor cells of the spinal cord. *Atropine* also paralyzes the motor centers of the organic muscular tissue. It stimulates the cardiac motor and respiratory centers, and produces rise of temperature.

PART III.

THE THERAPEUTICAL ACTION OF ERGOT.

PREPARATIONS AND ADMINISTRATION OF ERGOT.—The pharmacopœias of different countries do not give the same preparations of ergot, and the same preparations are not prepared alike. Ergot is used in powder, as fluid extract, extract, tincture, wine, infusion, sclerotic acid, etc.

The *powder* is hardly ever used in this country, but more frequently on the continent of Europe. Its taste, local irritating properties, uncertainty of strength, and comparatively slower action are the main objections to its use. The dose is 10 to 30 grains. The *fluid extract* is officinal only in the United States and British pharmacopœias, and is the commonest preparation in both countries. One minim represents, as usual, one grain of powder; but, as it is free from many irritating ingredients of the crude drug, it can be given in much larger quantities, and more frequently. The dose is from one half a drachm upward, according to the effect produced and the tolerance of the patient. Properly diluted, it can be used for hypodermic injections or external applications. It is of a dark-brown color; its taste and smell resemble those of the crude drug, but in a lesser degree. Beef-tea disguises its taste almost entirely. According to the United States Pharmacopœia, it is obtained by exhausting the powder with water, alcohol, and acetic acid. Formerly glycerine was also used. In England the fluid extract is obtained by treating the powder with ether, water, and alcohol. The *extract* is a very common preparation in this country and England, but it is officinal only on the European continent. It is prepared according to Bonjean's method, at times with some

modifications. It is called frequently Bonjean ergotine, or ergotine. The crude powder is exhausted with water; the solution is then evaporated to the consistence of syrup; alcohol is added; and after one day the mixture is filtered and evaporated to the consistence of an extract. It is used in pills, suppositories, ointments, and bougies, and, in solution, internally, externally, and hypodermically. The usual extracts represent about five times their bulk of the crude drug. The *tincture* is an antiquated preparation, although found in nearly every European pharmacopœia. Its strength is variable. The *wine* is officinal in this country. It is made by adding one part of the fluid extract to seven parts of sherry wine. It is very rarely used. The *infusion* is hardly ever used, although it figures on the list of the officinal preparations of nearly every country. In France ergot is prescribed also in the form of *syrup* (Sonbeiran's and Major's formulæ), *pill* (Bouchardat's formula), and *potion*. *Sclerotic acid* is not admitted yet to any pharmacopœia, but it is gradually gaining the favor of the profession. Representing the minimum bulk, acting the least as an irritant, and possessing all the desirable properties of the usual preparations of ergot, it bids fair to supersede them all at a not very distant period. Its use is rather common in Germany. The dose of sclerotic acid is from half a grain to one grain.

It is evident that the list of the officinal preparations is unnecessarily large and cumbersome, and might with advantage be reduced to the extract, the fluid extract, and sclerotic acid, for they are the only actual and practical modes of administering the drug.

For local applications either of the extracts can be used. As both are irritating, they must be diluted according to the requirements of the case. Five to ten per cent. will be found the most acceptable strength in the majority of cases. Any of the usual diluents can be used for this purpose.

For hypodermic administration we can use the extract, the fluid extract, or sclerotic acid, diluted in water with or without the addition of glycerine or alcohol. There is no evidence that the two latter substances improve the solution in the least. All precautions should be taken to have the solution always clear, and also not too

old. If the injections are particularly painful, the solution should be made a little alkaline. Injections must be practiced invariably in the muscular tissue. It is well also to begin with small doses to avoid the occurrence of any unpleasant accident.

We have stated that the physiological actions of ergot, digitalis, and strychnine have many points of resemblance, while the differences existing between them are such that one may correct the effects of another. In consequence, great benefit may be derived from associating these remedies together. Thus, digitalis will remove any objection that can arise on account of the sedative action of ergot on the heart, should the latter effect be contraindicated. The stimulating action of strychnine on the general nutrition will tend to neutralize the ill effect in this direction produced by the prolonged use of ergot. On the other hand, the combined administration of these drugs will intensify the specific action of ergot on the motor centers of the inorganic muscular tissue.

Chemical Incompatibilities.—Ergot should not be prescribed in combination with substances containing tannic acid, or with the metallic salts.

GENERAL INDICATIONS FOR THE USE OF ERGOT.—As the main feature of the physiological action of ergot is stimulation of the motor centers of the organic muscular tissue, its therapeutic uses must be intimately related with the morbid conditions of the organs composed of this tissue, or with those that can be relieved by acting on these organs. All other peculiarities of the physiological properties of ergot are of little or no practical value at all. In view of the exceedingly varied and numerous therapeutic uses of ergot, to facilitate this description it is well to place all similar conditions together and thus form a number of groups bearing their own distinct clinical type. Accordingly we have:

1. Disorders of the circulation, and diseases of the organs of circulation.
2. Paretic conditions of the organs composed of organic muscular tissue, the circulatory system excepted.
3. Inflammatory and other morbid enlargements and growths.
4. Abnormal secretions.

5. Symptoms referable to the nervous system, and depending chiefly upon the circulatory disorders within it.

As the only object of this classification is a practical one, we may overlook its numerous defects from the theoretical stand-point.

CONTRAINDICATIONS TO THE USE OF ERGOT.—Admitting the question of individual idiosyncrasy, which arises in connection with a great many drugs, we will mention here only the relation of ergot to such factors as the peculiar conditions of the heart, uterus, general nutrition, etc. A few years ago Dr. Thomson * raised the question whether ergot could safely be administered to a patient suffering from some serious cardiac disease. Having referred to the marked depressing action of ergot on the heart, he related a number of instances in his practice in which he thought sudden death was caused by the cardiac paralysis induced by ergot taken for a disorder entirely foreign to the heart. In the course of the discussion Dr. Bennett and Dr. Simpson coincided in the opinion that there was no sufficient evidence to ascribe the unfortunate termination in these cases to ergot. Granting the difficulty of deciding in each given case the merits of the point raised by Dr. Thomson, there can not be the slightest doubt that we must administer ergot with extreme caution to a patient with an enfeebled heart. Should it be borne badly, the combination with digitalis would present the best method for its use. In some cases ergot produces a particularly pernicious effect on the heart. Meadows reports a case in which attacks of angina pectoris were observed † every time it was taken. We have already referred to the fact that ergot is apt to produce very severe uterine colics in some women. If its combination with opium be undesirable or ineffectual, this will prevent the further use of the drug. Pregnancy is not an absolute contraindication, as there are cases on record in which ergot had been taken for a long time without interfering with gestation.‡ The use of ergot should be suspended temporarily dur-

* "Brit. Med. Jour.," Aug. 24, 1872.

† "Practitioner," 1875, p. 161.

‡ Semple, "St. Louis Med. and Surg. Jour.," Aug., 1875. Rouge, Nebinger, *et al.*, "Berl. klin. Woch.," 1873, pp. 531, 542.

ing menstruation unless it is given for some special condition of that function. If ergot is called for, and the patient's general health is very poor, it must be given per rectum or hypodermically, to avoid making matters worse by disturbing the digestion. By combining it with strychnine and digitalis, we place ergot in the most favorable conditions. We may state here that the rectal administration of ergot in suppositories, or as an enema, should be adopted in all cases where it is practicable.

ON THE USE OF ERGOT IN THE DISORDERS OF CIRCULATION, AND THE DISEASES OF THE ORGANS OF CIRCULATION.—We will consider first the circulatory lesions of the blood-vessels, namely, hyperæmia, congestion or vascular relaxation, acute and chronic inflammations.

Hyperæmia is a physiological condition of the blood-vessels characterized by an active peristalsis, producing a more rapid flow of blood, greater blood pressure, and increased transudation; the part in consequence is redder and warmer. Although this is the condition of the vessels when the organ is in a state of functional activity, it may assume a pathological character by being of an unusual severity, duration, and frequency of recurrence, or occurring in an abnormal place or at an unusual time, or if produced by abnormal causes, and is the source of some morbid manifestations. The symptoms of hyperæmia closely resemble those induced by irritation of the vaso-dilating nerves, and whether they are actually due to this or to paralysis of the vaso-contracting nerves depends upon the cause of the hyperæmia. At any rate, the treatment indicates the reduction of the violence of the circulation, and this is readily accomplished by ergot, which tetanizes and contracts the blood-vessels. Cold accomplishes the same result in two ways: directly, by making the vascular peristalsis more sluggish, and in a reflex manner, by acting on the sensitive nerves of the part. The astringents act chiefly in the latter way. Ergot acts from within, cold and astringents from without. The action of the first is a continuous one, while that of the latter is temporary, and requires repeated applications. Ergot has the advantage of being entirely free from any injurious influence on the morbid process itself, while the stimulants, from the very nature of their action, are apt to aggravate

it. But when the hyperæmia is deeply seated, the efficacy of external measures is very much reduced, if not entirely abolished, and we must use ergot, which can reach any part of the body. Reports relating to the treatment of hyperæmia with ergot are not very numerous in current literature, and they mainly relate to various morbid symptoms of the nervous system. The uniform success, and the nature of the physiological action of ergot on the blood-vessels, should lead to a more general use of ergot in this class of diseases.

Relaxation of the blood-vessels, or congestion, is another circulatory disorder, functional in its character, and the very reverse of hyperæmia. The vessels lose their tone, and peristalsis is absent or sluggish; they are not responsive to external agents, and remain relaxed, the blood flowing slowly and at a reduced pressure. If this parietic state is idiopathic, as it usually is, we must look for the primary cause in the lost vigor of the vaso-motor innervation, depending frequently upon the depressed state of the general health. General tonics, local stimulants, massage, electricity, hydrotherapy, etc., are the usual methods adopted in the treatment of this condition; and ergot, strychnine, and digitalis are the natural systemic agents to be used, because they meet in a direct manner the cardinal defect of the circulation.

The use of ergot in *inflammations* is a very important topic, considering how frequently we are called to treat the diseases depending upon it, and how inadequate at times our measures against it prove themselves to be. The latest researches on the pathology of inflammation show conclusively that it depends mainly upon the altered state of the walls of the blood-vessels. We may say in a general manner that the healthy state of the blood-vessels is compatible only with the normal circulation and the normal character of the blood. We are also gradually learning to appreciate the influence of trophic centers over the nutrition of the blood-vessels. The blood-vessels possess a certain tolerance of minor deviations from the normal conditions; but, once this limit is overreached, their nutrition becomes more or less seriously affected, giving rise to a variety of structural lesions, such as inflammation, fatty, atheromatous, waxy degenerations; other conditions determine infarctions, the hæmor-

rhagic diathesis, purpura, aneurism, etc. As the subject has been little studied, and is irrelevant, we will omit the consideration of the influence of the trophic centers. The question of the blood-changes has also no direct bearing on our subject. The quantitative blood-changes—the amount of the normal ingredients of the blood being lesser or greater—and qualitative blood-changes—alterations of the albuminoid principles, or the presence of foreign substances in the blood, such as lead, alcohol, the syphilitic and the malarial poisons, etc.—frequently cause structural lesions of the blood-vessels. The general tendency is to ascribe these lesions to the direct action of these blood-changes on the walls of the vessels, but the more correct explanation is, at least in the cases of the saturnine, alcoholic, and syphilitic intoxications, that they are of a central trophic origin, determined by the presence of the above-mentioned substances in the blood. The last element, the circulatory disturbances, is the most important for us, not only on account of its greater frequency as the cause of inflammation, but also because it relates to the antiphlogistic properties of ergot. Of these disturbances the deviations from the normal in the energy of the flow of blood are the most important.

Unfortunately, we can not trace minutely all the stages in the evolution of the inflammatory process. In some cases of reflex inflammation, as, for instance, when it attacks deep-seated viscera as the result of profound cutaneous irritation—from burning, the electric moxa, the application of blisters, etc.—there can hardly be any doubt that the first effect of the irritation is to cause an intense reflex anæmia in the organ; and, when the vascular spasm after a while becomes relaxed, and the circulation is restored, the blood no longer finds a healthy, normal vessel, but one changed from the prolonged starvation, in consequence of which arises the train of symptoms observed in the course of inflammation. But the latter may also originate in an entirely different manner; namely, instead of the preceding stage of anæmia, it may proceed from an excessive hyperæmia. Let it be too intense, or last a considerable length of time, and shortly the unnatural energy of the circulation becomes the cause of altered nutrition of the vascular wall; it ceases to react

in the natural manner to the blood within, and so-called inflammation sets in. If we take the extreme examples of both types of the vascular lesions, it is evident that they are not identical, otherwise no material difference can be detected. Once the inflammation is established, in the central focus of the affected part we find the inflammatory changes in the vessels at their height, while in the centrifugal direction they are less marked until we reach the border, where there is little beyond pure hyperæmia. This coëxistence of hyperæmia and inflammation is very important to bear in mind, as the first serves as the fuel to the latter, and, unless the functional disturbance of the circulations subsides of its own accord, or from the remedial agents directed against it, the structural lesions of the blood-vessels can not but progress. In fact, the largest area of every inflamed region is composed of the hyperæmia; here the color is of a brighter hue, and the part is warmer, but it is less hard, tumefied, and painful than at the main seat of the structural lesion. The microscopical aspects present a greater difference; the inflamed vessels do not pulsate, they are relaxed; do not respond to external stimuli, their physical properties are altered, as is seen from a certain tendency on the part of the white corpuscles to adhere to them, the ready transudation of the fluid portions of the blood through their walls, and the escape of the corpuscles. Absent peristalsis determines slower blood current, which is impeded still further by aggregation of the white corpuscles along the walls. Let this state continue long enough, and the change within the parietes of the vessels will reach the point at which the latter will become entirely unfit to perform their function; circulation stops, the surrounding tissues break down, and a slough is the final result. But if the retrograde process becomes established, hyperæmia subsides, the circulation assumes its normal character, and, with the access of healthy blood, the blood-vessels that did not suffer irreparably will gradually resume their function, and the part will be healthy once again.

We conclude from the preceding considerations that the only rational treatment of inflammation is one which is directed against the hyperæmia and the violence of the circulation within the affect-

ed region. If we now examine the therapeutic properties of the measures, general and local, which daily experience has proved to be efficacious in the treatment of inflammation, we readily appreciate that, in every instance, they tend, in one way or another, and more or less directly, to reduce the amount of the blood in the part, to diminish the violence of its circulation, or, in other words, to meet the indication which we have just mentioned. Such are the ultimate results of using cold, counter-irritants, revulsives, local and general depletion, and mechanical measures like postural treatment and compression; and they are still more readily obtained if the local treatment is assisted with purges, vascular sedatives, anodynes, rest, etc. With our present knowledge of the action of ergot on the circulation, and with a clear idea as to what we wish to accomplish in treating an inflammatory disease, we shall naturally be inclined to estimate the antiphlogistic properties of ergot highly. The indications for its use are rational, clear, and based upon positive knowledge of the object and means. There are innumerable instances of therapeutic uses of drugs in general practice upon bases far less sound and firm than the claim just advocated. The value of ergot becomes still greater if we are dealing with a deep-seated inflammation, too far from the surface to be reached by, or of a nature precluding the use of, the greater part of the above-named local measures.

We have dwelt, so far, upon the local action of ergot, but every grave inflammatory process is accompanied by marked constitutional symptoms, which call for attention, sometimes even more urgently than all the local manifestations combined. Fever, violent beating of the heart, headache, and disturbed sleep from the hyperæmia of the brain, leading sometimes to delirium, and rapid respiration, are the common features calling for relief. We know already, and further proofs will be presented later on, that ergot will quiet the heart, relieve cerebral congestion, reduce the temperature, and diminish the frequency of the breathing. Taking, then, the whole action of ergot on the system in case of an inflammatory affection, we must pronounce it an antiphlogistic *par excellence*, as it meets in a direct manner every element of the inflammatory process.

And if we bear in mind that it in no way conflicts with anything else we may adopt at the same time, but, on the contrary, that it insures a more efficacious action of these measures, we acquire an additional reason to use it in this order of diseases. The course of an acute inflammation, as a rule, is brief, and there can be no danger in using frequent full doses of ergot. The hypodermic method, injecting in the immediate vicinity of the diseased part, may be adopted if it is desirable. Smaller and frequently repeated doses are to be preferred to a few large ones. The inflamed surfaces may be treated also by some liquid preparation of ergot, if this is deemed necessary.

So much for the theoretical consideration of this subject. If we look now over the past volumes of the medical periodical literature of different countries, we find that a large number of physicians have been led, by one reason or another, to treat different inflammatory diseases with ergot. Their reports, which will be laid before the reader in as condensed a form as the nature of the subject will permit, will convince him, by their uniformly favorable character, of the correctness of the argument just advanced.

Croupous Pneumonia.—Up to a very recent date we were taught with regard to the treatment of pneumonia that "Nature cures, and the only duty of the physician is to maintain life until this cure is effected." * But the recently conducted experiments with the calomel treatment in the hospitals of this city have clearly demonstrated that we can modify the course of the disease materially and favorably. It is opportune, then, to discuss the merits of another radical method of treating the same disease, the advantage of which lies in the absence of the pure empiricism peculiar to the calomel treatment. Wycisk,† Herminades,‡ Searce,# Yeaman,|| Wells, ^ Boggs, ◇ C.

* Jürgensen, von Ziemssen's "Cyclopædia," v, p. 150.

† "Allgem. med. Central-Zeitung." "Phila. Med. and Surg. Reporter," xxxii, 1875, p. 447.

‡ "Nederl. Tijdschr. voor Genesk.," 1874, p. 34. Virchow and Hirsch, "Jahresbericht," 1874, i, p. 487. # "Phila. Med. and Surg. Reporter," xxxvi, 1877, p. 299.

|| "St. Louis Clin. Record," 1878, p. 280. ^ "Med. Record," 1879, p. 405.

◇ "Brit. Med. Jour.," 1879, ii, p. 772.

Handfield Jones,* Hobbs,† and Meacher and Colman‡ unanimously affirm that ergot, particularly if given early in the disease, can abort it, make it of a shorter duration, or make it of a milder severity with regard to its general and local symptoms, the expectoration assuming almost immediately a pale color and diminishing in quantity, the cough lessening in frequency and severity, the fever soon receding in intensity, and the convalescence being very rapid. For my own part, I have been able to verify the truth of these statements, and some of my friends who have been induced to try the treatment also speak favorably of its efficacy. The rapid and invariable decoloration of the sputa speaks conclusively in favor of the pulmonary circulation being effectually attacked by ergot. In view of the importance of the subject, the reader will pardon me for transcribing the report of Yeaman's case, as it illustrates very typically the action of the drug in this disease.

December 13th, 9 A. M.—Forty-eight hours after rigor, patient aged thirty, male. The general signs of the disease, as dullness, crepitant râle, bronchial breathing (in opposite lung), rusty sputum, dyspnœa, etc., are well marked. Temperature 104·5°, pulse 108. Had taken, before I saw him, a large dose of calomel, which moved the bowels freely several times. 12 M.—Commenced taking ergot, fl. extr. 3 ss. every two hours. Temperature 105·5°, pulse 116. 4 P. M.—Temperature 105°, pulse 112.

December 14th, 9 A. M.—Temperature 104°, pulse 104. The medicine was taken several times during the night. Dyspnœa less troublesome, sputum contains less blood, cough much less painful and frequent. Sweat profusely for two hours early this morning. Skin moist. The medicine has produced stupor, patient easily aroused. No pain when quiet. Ord. R̄ Ammon. muriat. ℥ ij, syr. scillæ, glycerinæ, āā, ʒ j. M. S. Desertspoonful every two hours. 12 M.—Temperature 103°, marked improvement in every way. 4 P. M.—Temperature 102·25°, pulse 100. Drowsiness increased. Expectoration very slight, and free from blood. Apparently suffers no pain whatever.

December 15th, 9 A. M.—Temperature 101·5°, pulse 108. Has eaten nothing for sixty hours; ordered beef-tea and chicken broth. 3 P. M.—Temperature 100·5°, pulse 100. Skin moist and cool; constant stupor. 8 P. M.—Discontinue ergot till morning.

December 16th, 9·30 A. M.—Temperature 99½°, free from pain, and inclined to

* "Brit. Med. Jour.," 1879, ii, p. 856. † "South. Med. Record," ix, 1879, p. 401.

‡ "Chicago Med. Jour. and Exam.," 1880, p. 260.

be jocular; ergot, ten drops every two hours. 4 P. M.—By a misunderstanding, no ergot since yesterday evening; temperature 101.25° ; ordered 3 ss. doses to be given again, and to be taken during the night.

December 17th, 9 A. M.—Found patient up, eating breakfast with his family.

It is evident that ergot did not cut short the actual duration of the disease; but, from the record of the temperature, it is apparent that its action upon the severity of the inflammation was immediate and progressive. Exacerbation occurred only once, and this was due to the medicine being omitted for a considerable length of time.

C. Handfield Jones's case demonstrates also a marked reduction of the temperature:

Beginning of the disease on May 16th, admitted to the hospital on the 19th. Temperature 104° , pulse 96, respiration 47. Ordered 3j fl. extr. of ergot four times a day, also ʒj mist. ammon. acet. Rapid improvement from that time on.

May 20.—Temperature, 102.9° ; pulse, 102; respiration, 48.

" 21. " 100.7° ; " 86; " 33.

" 22. " 98.6° ; " 78; " 44.

" 23. " 97.8° ; " —; " —.

" 24. " 97.8° ; " 66; " 34.

Wounds.—Here is another excellent opportunity of observing the action of ergot on the inflammatory process. Flourens,* Bonjean,† Labat,‡ and a great many French # and Italian physicians || have used it internally or as a dressing in the treatment of wounds. According to them, ergot tends to make the wound heal more kindly; to diminish the suppuration; to combat the inflammation about it; and to reduce the liability to blood poisoning. Ergot had been used very extensively during the Crimean campaign with the result of establishing on a firm basis its hæmostatic and anti-putrid properties for local applications. It had been frequently incorporated in the dressings for inflamed and bleeding wounds to control profuse and unhealthy suppuration occurring after severe injuries, and also in the treatment of scorbutic, irritable, scrofulous, and chronic ulcers.△ Pirogoff◇ recommends ergot dressings also in the treat-

* "Wien. med. Woch.," 1865, p. 451.

† "Comptes Rendus," 1867, p. 1100.

‡ Labbé, "Gaz. des Hôp.," 1867, p. 5.

"Berl. klin. Woch.," 1869, p. 133.

|| "Wien. med. Woch.," 1865, p. 451.

△ *Ibid.*

◇ Pirogoff, "Voyenno-polevaja Chirurgia," Dresden, 1865, i, p. 336.

ment of bleeding wounds in exhausted, scorbutic, or pyæmic patients. Of course, since the introduction of our modern antiseptic and improved dressings, wounds only seldom assume the grave character so common formerly; yet very frequently they succeed only partially in eliminating every source of irritation and inflammation, so that, by accepting the experience of the past, we may still derive benefit from the local use of ergot. Brown * has reported a case of an obstinate cold abscess cured by repeatedly washing it out with infusion of ergot. Flourens finds a two- to five-per-cent. solution of ergotin in water best for ordinary wounds, and a five- to ten-per-cent. solution for hæmostatic dressings.

Inflammatory diseases of the skin allow us to watch closely the behavior of the morbid process under the local or internal use of ergot. Sovet † found it useful in all inflammatory diseases of the skin; also in erysipelas. Eldridge ‡ more recently treated a number of cases of acne rosacea, of alcoholic and other types, by means of local applications and injections into the affected skin, invariably curing the disease. For hypodermic purposes he used the following solution: R Extr. ergotæ, gr. xv; glycerinæ, 3 ss.; aquam ad 3 ij. M. Of this, he injected two to three minims every third day. Still more recently, Denslow * has found 3 ss.-doses of the fluid extract three times a day very beneficial in the same disease. Piffard | failed to see any benefit in a case of rosacea from a like treatment. Fox ^ states that ergot taken internally seems to improve some cases of acne; but, in one case of rosacea in which he used it, no improvement was noticed. Meyerhoff ¶ obtained great results from local applications of ergot in varicose ulcers and eczema. I have treated a case of an obstinate facial erysipelas of two months' standing, and covering one side of the face, with an ointment of vaseline containing three per cent. of the extract of ergot and digitalis. A very striking improvement was noticed within twenty-four hours, the disease being entirely cured in ten days. Subsequent relapses

* "Lancet," May, 1849.

† "Bull. Gén. de Thérap.," xxxii, 1847, p. 330.

‡ "N. Y. Med. Jour.," Oct., 1879, p. 360.

* *Ibid.*, Feb., 1881.

| *Ibid.*, Aug., 1881, p. 184.

^ *Ibid.*

¶ "Dtsch. med. Woch.," 1881, No. 8.

were treated in like manner; dispersing the inflammation in a few days. The same ointment, alone or in conjunction with Hebra's diachylon ointment, acted well in eczema attacking the legs, and in chronic ulcers with eczematous borders. Riedinger* injected ergotin into the substance of a frozen nose, controlling the inflammatory process in a striking manner.

Inflammations of the mucous membranes have been frequently treated with ergot, taken internally or applied locally, as the case may be. Sovet (*loc. cit.*) used it with benefit in ophthalmia. Planat† obtained also good results in different forms of ophthalmia. He used a five- to a seven-and-a-half-per-cent. solution of ergotin in glycerine or rose-water, from 8 to 10 drops to be put into the eye every two hours. If chemosis is present, or inflammation is very severe, he recommends to place over the eye compresses soaked in the same fluid.

Dabney‡ is less pleased with ergot in acute ophthalmia, or when there is a good deal of irritation, than in less active inflammation, and particularly when there are present large, tortuous blood-vessels. He uses a solution of 10 grains to the ounce of water with one drachm of glycerine. The eye is washed a number of times a day with warm water, and a few drops of the solution placed in it. He believes ergot has been used with benefit also in granular conjunctivitis. He makes daily applications with a camel's-hair brush of a solution of ergot thrice as strong in cases of pharyngitis. Also better results are obtained in chronic forms. He combines in some cases 3j of tincture of iodine with ʒj of ergot solution. Eldridge (*loc. cit.*) reports a number of cases of gleet and gonorrhœa rapidly cured by applications of the extract to the urethral mucous membrane. Also a case of chronic otitis, treated locally with extract of ergot a little diluted with glycerine, rapidly improved after eight applications. T. Curtis Smith# obtained a good result in a case of severe chronic bronchitis; ergot was taken internally. Ergot may

* "Arch. f. klin. Chir.," 1876, p. 457.

† "Med. Record," 1879, p. 528.

‡ "Am. Jour. of the Med. Sci.," July, 1879, p. 101.

"Phila. Med. and Surg. Reporter," xxxii, 1875, p. 445.]

be said to be a specific for cystitis, particularly in its chronic forms, leucorrhœa, uterine or vaginal, diarrhœa, and dysentery. These will be referred to more fully later on.

Ergot has been used with benefit also in *inflammations of the serous membranes*. Gibney and Caro * had good results from it in *tubercular meningitis*. A case of *cerebro-spinal meningitis* is reported cured with ergot.† Read ‡ reported also good results from it in the same disease. In fact, ergot is used quite frequently in all forms of meningitis.

Ergot also exerts a very favorable action if inflammation attacks different organs, as we have seen already, as an instance, in the case of pneumonia. Schtscherbinkoff, # having witnessed complete suppression, or a considerable diminution, of milk in women and cows during the epidemic of ergotism occurring in Simbirski district (Russia), was led to try it in cases of threatening mammary abscess, so-called milk-fever, enlargements of the breast accompanied by fever aside from the puerperal state, and also in local disorders following the weaning of the child; and the results were invariably good. Ergot, as the reader is aware, is the standard remedy in nearly all forms of myelitis. T. Curtis Smith (*loc. cit.*) observed beneficial results from its use in a case of chronic pneumonia. Phthisis has been frequently treated with ergot by French physicians, and the symptoms were more or less improved by it. To this testify Arnal, Gauillaud, Piedagnel, Seé, and others. || Planat (*loc. cit.*) speaks favorably of local applications of ergot in iritis. It is used very extensively at present, particularly in Germany, for different inflammatory diseases of the uterus. Manette ^ speaks well of ergot in adenitis and orchitis.

It is needless to say that the foregoing examples of the use of ergot in the treatment of inflammatory diseases are only a portion of what is buried in past literature, but they are more than suffi-

* "Phila. Med. Times," viii, p. 66.

† "Boston Med. and Surg. Jour.," July 18, 1867.

‡ "Phila. Med. and Surg. Reporter," xxx, 1874, p. 556.

"Centralbl. f. Chir.," May 8, 1875. | "Wien. med. Woch.," 1865, p. 451.

^ "Med. Brief," 1877, p. 349.

cient to remove any doubt the reader may have had with regard to the merits of the theoretical considerations advanced in the preceding pages. The list of the diseases referred to is a very large one embracing a considerable portion of special pathology, but they are simply different manifestations of one and the same process—inflammation; and ergot cures, relieves, and improves them only in so far as relates to it alone. From the humblest to the most eminent members of our profession comes the invariable testimony that ergot exerts a favorable influence on the inflammatory process. Its merits have been tested during more than a quarter of a century, although most frequently during a more recent period, in nearly all countries, and by persons generally ignorant of the experiences of others in the same direction; only a very few were aware of similar efforts in the same field. Consequently this unanimous verdict can not be considered a representation of some single local school, nor as expressing some transient movement in science, but should be looked upon as an unbiased and confirmed conclusion, which we must accept, whatever may be the merits of the individual cases referred to. The reader may have noticed that ergot has been used frequently in diseases of minor practical importance, but only seldom in such as task all our resources. This is natural, considering the experimental nature of the first efforts, but we can, in the present state of this question, assume a more definite position, and resort to ergot with less doubt as to its efficacy than formerly.

We have spoken, so far, only of the use of the drug in acute inflammation. Chronic inflammation presents even more favorable conditions in some respects than the former. Like the acute form, it originates also in functional circulatory disturbance, which is in this case of a parietic character. Eventually the abnormal conditions of the blood current and of the blood itself react upon the nutrition of the parietes of the vessels and of the adjoining tissues, producing the lesions peculiar to this variety of inflammation. If the part affected is situated within the reach of local measures, which are very much the same as we use in the acute process, there is a possibility of restoring it to health; but even in such cases the treatment is frequently very protracted, and at times fails entirely.

When less favorable conditions are present, we know, from past experience, the disease is beyond our means, and we limit our efforts to controlling the symptoms it gives rise to. Among the cases illustrating the action of ergot on the inflammatory process we have included a number of diseases of chronic type, and the results have been fully as favorable as in the acute disease, and at times even better, on account of the lesser irritation and the milder lesion of the blood-vessels permitting a more liberal use of the drug, if applied locally, and a readier response to it on the part of the blood-vessels. Of course the results will be the better the earlier in the course of the disease the treatment is resorted to.

Our knowledge of the pathology of *purpura* is too imperfect to give us any clew to a rational treatment of this disease. The drift of the present evidence is to the effect that it is of tropho-neurotic origin. Circumscribed hæmorrhages in different parts of the body, and other evidences of a diseased state of the blood-vessels, occur frequently in the course of the diseases of the central nervous system, or in consequence of injuries to these centers.* Lewaschow, † subjecting the large nerve-trunks to a prolonged mechanical irritation, obtained in every case lesions of the blood-vessels supplied by these nerves, apparently identical with those of *purpura* as they are described by Hayem and Orion. ‡ On the other hand, *purpura* is anything but a local disorder. We find it in connection with acute or chronic rheumatism; it occurs frequently in persons with the rheumatic diathesis, or in the course of scurvy. As a spontaneous disease (*morbus maculosus*) it is, again, a constitutional disorder, the entire course of which can be made intelligible only on the basis of its being due to a morbid state of the trophic centers regulating the nutrition of the blood-vessels. This supposition is far more in accord with the facts of the case than the theory that the changes of the blood-vessels are secondary to some morbid state of the blood. These theoretical considerations are laid before the reader because they relate to a property of ergot

* Charcot, "Diseases of the Nervous System," 1879, p. 85; Nothnagel, "Centralbl. f. d. med. Wissensch.," 1874, No. 14.

† "St. Petersburg. med. Woch.," 1880, No. 31. ‡ "Rev. des Sci. Méd.," xvi, p. 161.

not apparent when we study its physiological action, but which becomes evident when we examine its therapeutical action, namely, that it modifies the nutrition of the blood-vessels. Only from this stand-point can we understand why it should be so beneficial in purpura,* and in a number of other diseases of the blood-vessels to be spoken of presently. Hypodermic injections in the affected part cut short the disease, and the effusion of the blood rapidly passes away.

The use of ergot in the treatment of *aneurism* is a very important and interesting chapter of the therapeutical action of the drug. Although the priority of adopting it in this disease is conceded to Langenbeck, I find it mentioned that ergot was used in aneurism by a number of French physicians at an earlier date than that of the report of Langenbeck's cases.† His intention in using ergot was to act on the muscular structure of the sac, and thus to reduce the size of the tumor. The results obtained were excellent, but the *motive* can not be sustained. The history of his two cases is as follows:‡

I. An aneurism of the right subclavian artery, of five years' standing, of the size of a man's fist. Hypodermic injections of ergotin (0.5–2.88 grains) every fourth day between the skin and the tumor. In all 30 grs. were consumed during six weeks. The improvement was immediate and progressive, and when the patient was exhibited before the Berlin Medical Society the size of the tumor was much diminished, the pulsation was very slight, and he was able to use his arm.

II. Traumatic aneurism of the radial artery at the wrist joint, of the size of a hazel-nut. After one injection the tumor disappeared entirely within twenty-four hours. The treatment was begun immediately after the injury.

* Bauer, "Dtsch. Klinik," 1868, p. 313; Henoeh, "Berl. klin. Woch.," 1868, No. 50; Piazza, Virchow u. Hirsch's "Jabresb.," 1874; Mavor, "Brit. Med. Jour.," Oct. 31, 1874; Lewes, *ibid.*, p. 690; Lane, *ibid.*, Sept. 5; Minich, "Phila. Med. Times," 1874, p. 502; Bulkley, "Practitioner," 1876, p. 323; Monette, "Med. Brief," 1877, p. 349; and many others.

† "Wien. med. Woch.," 1868, p. 126.

‡ "Berl. klin. Woch.," 1869, pp. 117, 133.

The solution used in both cases consisted of one part of ergotin to three parts, each, of alcohol and glycerine.

Schneider* reported to the Medical Society of Königsberg a permanent cure of an aneurism of the femoral artery, treated like Langenbeck's first case. No details are given.

Albanese† reported a very interesting case, which illustrates the mode of action of ergot in these cases. An aneurism of the innominate artery, of the size of a mandarin orange. The tumor dated back about six months. After the third injection the pulsation became feeble and the size of the tumor perceptibly smaller. On the fifth day of the treatment the patient was able to move her head and arm more freely, and the respiration became easier. After four more injections the decrease of the tumor became still more noticeable, with corresponding improvement in all the symptoms. On continued injections, which were made at longer intervals, her condition steadily improved; she could be out of bed and could speak without any difficulty, and the swelling of her arm passed away entirely. At the end of a month of the treatment, finding herself very much better, she left the hospital.

Dutoit's‡ case resembles somewhat the preceding case. Here the injections were combined later on with compression of the tumor. Recovery. A large circumscribed aneurism of the left sub-clavian artery. After four injections, practiced every second or third day, a very marked decrease of the tumor was obtained. The improvement continued. After one month of treatment he applied interrupted digital compression for a week, and later on he adjusted an apparatus to exert a uniform pressure over the tumor. The injections were continued. The cure was obtained in five months.

Herminades# cured a popliteal aneurism. Wolff|| cured an aneurism of the abdominal aorta. Tilanus (reported by Herminades)

* *Ibid.*, p. 390.

† "Gazz. Clin. di Palermo," 1870, No. 1.—"Brit. and For. Med-chir. Rev.," xlvii, p. 239.

‡ "Arch. f. klin. Chir.," 1871, p. 1070.

* *Loc. cit.*

|| "Berl. klin. Woch.," 1873, p. 314.

has had only partial success. Range and Quincke met with failure, while Catiano's patient recovered.* Plagge† used the injections for a traumatic aneurism of the femoral artery. The tumor decreased in size; digital compression was resorted to; the patient recovered. Carter‡ treated a thoracic aneurism with iodide and bromide of potassium, later on with injections of ergotin, diet and rest through the entire course of the treatment. In three months the patient's condition was very much improved, pulsation was scarcely perceptible, and the murmur was almost inaudible. He left the hospital, but returned three months later in a worse condition than before; the cure was accomplished by galvano-puncture. Sutton§ treated a case of aneurism of the descending portion of the arch with the fluid extract of ergot, iodide of potassium, and rest. The treatment lasted thirteen months, and resulted in a perfect cure.

Ord|| employed ergot in three cases of aneurism. In two cases of thoracic aneurism the administration of ergot was always followed by the improvement of all the symptoms; the effect was immediate, but the treatment was not sufficiently systematic and long-continued to give any permanent results. The third patient, with abdominal aneurism, apparently recovered entirely. Ergot was used internally.

Stephens^ had also favorable results in a case of an internal aneurism. No details given.

The foregoing cases are sufficient in number to establish the merits of ergot. It can hardly compete with operative measures in the treatment of the peripheral tumors, although, as we have seen, cure was also obtained here. Its legitimate field is that of the internal aneurisms, against which we have so far nothing to offer with any certainty of success. Galvano-puncture is efficient only under certain conditions, of which we can not be conscious in advance.

* Quincke, von Ziemssen's "Cyclopædia," vi, p. 453.

† "Memorabil.," xviii, 10, p. 441.

‡ "Lancet," 1878, ii, p. 761.

§ "Am. Jour. of the Med. Sci.," Oct., 1880, p. 454.

|| "St. Thomas's Hosp. Rep.," x, p. 191.

^ "Cincinnati Lancet and Clinic," Aug. 27, 1881, p. 182.

On the other hand, it fails to produce the slightest influence on tumors apparently presenting the very conditions most favorable for its use. What is more, it is not a measure entirely free from dangers. From the histories just presented it is evident that ergot acts more promptly and effectually than iodide of potassium, and, as Sutton's and Carter's cases show, both drugs can be used at the same time. Although we have a number of cases of aneurism treated with ergot, we can not yet draw any conclusions with regard to its powers. As we have seen, a number of failures are recorded (Range, Quincke), but, having no details, we can not judge of the merits of these negative results. We know that if ergot treatment is not of a sufficient duration the effect is only temporary, and the disease returns with the former severity, while, on the other hand, if the treatment was persisted in, the cure was accomplished. Not wishing to proclaim ergot as a specific against aneurism, I am still inclined to think that the partial or entirely negative results may have been due to the improper use of the drug as well as to the limited possibilities of the treatment itself.

To be in the position to obtain the maximum benefit from any drug we must fully understand the mode of its action. In view of the importance of this subject, the reader will pardon me for reviewing some of the reported cases. Langenbeck thought that ergot acted on the muscular tissue of the sac. But this is untenable, because the muscular tissue is very scanty in the coats of the larger arteries, and its amount becomes still smaller under the influence of the inflammatory and degenerative processes resulting in the formation of the sac. So that the action of ergot on this tissue can not be of much value in reducing the size of the tumor, and it may be entirely excluded from consideration. The suggestion of Schwalbe,* that the hypodermic injections of ergot cause an irritation and subsequent connective-tissue hyperplasia in the vicinity of the tumor, thus strengthening its walls, is simply absurd, because this can not account for the decrease in the size of an aneurism. What is more, ergot produces the same effect if it is injected at a distance from the

* "Arch. f. path. Anat. u. Physiol. u. f. klin. Med.," lvi, p. 360.

tumor, or if taken by the stomach. Besides, its action is too rapid and marked to be explained in such a manner. In every case of which we have a detailed account, we find that the tumor diminished in size in a few days after the beginning of the treatment, and frequently this occurred as soon as the full physiological action of the drug became manifest. In Ord's cases this was particularly noticeable. In the first case (a thoracic aneurism) the plaster cast of the tumor fitted it loosely after the systemic action of one dose of ergot had had time to show itself. In the second case (an abdominal aneurism), seventeen minutes after taking a dose of the medicine the dimensions of the tumor decreased one inch vertically, three quarters of an inch transversely, the beats became equalized, the murmur almost ceased, and the range of the pulsation became smaller. The decrease in the violence of the pulsation in the sac showed itself very early in all the cases. These two changes—the decrease of the size of the tumor and of the force of its pulsation—are, then, the immediate effects of ergot, and are due to the reduced pressure and tension within the sac, depending in their turn upon the sedative action of the drug upon the heart. Only Wolff had taken pains to note the frequency of the pulse rate before the beginning of the treatment and at the time of the discharge of the patient, the reduction being from 82 to 64. But, from what we know of the action of ergot on the heart, this effect must be present in all cases. This alone can be the cause of a marked palliation in the severity of the symptoms, and if the tumor is well sacculated, communicating with the lumen of the vessel by a narrow opening, the prospect of cure by a gradual deposit of fibrine is rendered very favorable. Still, even in such cases a long time will be required before permanent benefit will take place, and, consequently, the patient should be kept under the influence of ergot, although no apparent further change in the appearance of the tumor is noticeable. To give the patient every chance he is entitled to, ergot should be combined with rest in bed and proper dietetic regulations. It is better also to combine ergot with iodide of potassium.

But, does the sedative effect of ergot on the heart constitute its entire action in cases of aneurism? This seems to me very doubt-

ful, and for the following reasons: It is impossible to assume that all cases cured by ergot, and the number exceeds that of the failures, were such as to be cured by decreased arterial tension alone. The cure of an aneurism is too complicated a process to depend alone upon the state of the blood pressure. Iodide of potassium, whose beneficial action in aneurism is well established, acts upon the circulation to a very slight degree, although a diminished action of the heart and a relaxed state of the arteries are among the symptoms of iodism. When the system is brought well under its influence we observe numerous indications of its acting also upon the walls of the blood-vessels—iodic acne, ecchymotic and hæmorrhagic foci in the skin and the internal organs. It would seem, then, very plausible that these two agents have a direct action on the blood-vessels, and that to it as well as to their action on the circulation the improvement of aneurism is due. Should the former become more evident than it is at present, it will be an additional argument in favor of giving a fair and thorough trial to ergot, and not to abandon its use as soon as the disease becomes stationary.

Ergot has been used also in *varicose disease of the veins*. Vogt* was the first to suggest it. Subsequent experience was as favorable as his own.† Ergot was injected in the vicinity of the affected blood-vessels.

Bertarelli and Cittaglia‡ adopted the same treatment in *varicocele*. In the case of the former the varicosities disappeared on the second day after the second injection. The patient of the latter did not recover until the eighteenth day of the treatment.

The use of ergot in *hæmorrhoids* is rather common. They yield rapidly to injections of ergot made either near the anus or in the substance of the tumor; also to rectal suppositories containing it.‡

* "Berl. klin. Woch.," 1872, No. 10.

† Herminades and Tilanus, *loc. cit.*; Range, Nebinger, Goldschmidt, and Martin, "Berl. klin. Woch.," 1873, pp. 531, 542.

‡ "Med. Record.," 1874, p. 260.

* Semple, "St. Louis Med. and Surg. Jour.," Aug., 1875; Lansing, "Phila. Med. Times," Oct. 13, 1877; Dabney, *loc. cit.*; Lamadrid, "Phila. Med. Times," 1877, p. 48, and "N. Y. Med. Jour.," 1875, p. 275; Ferrand, "Rev. Méd. Franç. et Etrang.," Mar. 26, 1881.

Very good results have also been obtained in the treatment of *nævi* by Herminades and Hammond.* The latter injected ergot into the affected part itself.

The beneficial action of ergot in these different diseases of the blood-vessels can not be explained alone by what we know of its physiological properties. We must admit also, which is very plausible, that ergot has a power of modifying the nutrition of the blood-vessels.

Universal experience has established too well the value of ergot in arresting *hæmorrhages* to call here for anything beyond the mere mention of the subject. But we do not use it sufficiently often as a preventive when this accident is apt to occur. In all such cases ergot should be used during the entire critical period, and the reduced vigor of the heart's action, with the lowered arterial tension, will contribute largely to pass it safely. We have mentioned the local hæmostatic properties of ergot already, which are not well known to the profession. Schuberini and Becchis,† Flourens and Sédillot,‡ Bonjean,§ and others have found it useful as a local application to bleeding surfaces. Pirogoff considers ergot and chloride of iron as the only reliable topical hæmostatics. Dixon,|| by injecting a solution of ergotin into the urethra, arrested an obstinate hæmorrhage from that source. In former editions of the Russian pharmacopœia existed an officinal preparation—aqua hæmostatica Neljubini—prepared by exhausting with water and alcohol powdered ergot and a number of aromatics.^A I may mention in connection with this subject that Gröbenschütz◇ has found ergotin injections very efficient in arresting the oozing of the blood after the use of Esmarch's bandage, which is often so troublesome to check.

To close the subject of the use of ergot in the diseases of the circulatory system, it remains to say a few words of its value in *car-*

* "Arch. of Clin. Surg.," Oct., 1876.

† "Bull. Gén. de Thérap.," xlviii, p. 362.

‡ "Wien. med. Woch.," 1868, p. 125. § "Bull. Gén. de Thérap.," xxxvii, p. 137.

|| "Cincinnati Med. News," ix, p. 107. ^A Dybkowsky, *op. cit.*

◇ Inaug. Diss., Virchow und Hirsch's "Jahresb.," 1874.

diac affections. Its main indications in these cases are: excessive action of the heart; relaxation of its muscular structure, and hypertrophy.

We do not realize sufficiently the dangers of excessive action of the heart. And yet we should always recognize it and arrest it, as it leads invariably in time to degeneration and atrophy of the organ. This can be readily demonstrated on an animal by cutting both pneumogastrics, the cardiac paralysis supervening in a few days from exhaustion, and the organ presenting evidence of fatty degeneration of the muscular fibers. But such experiments are not so well adapted to the study of this question as the one proposed by Wassilieff,* consisting in inflicting upon these nerves various injuries which would only partially impair their inhibitory function; thus the life of the animal is prolonged, and we can observe better the natural consequences of the over-action of the organ. According to Wassilieff, the hearts of animals thus treated suffer invariably from a fatty degenerative process, the intensity of which is in proportion to the duration of the experiments. Eichhorst explains these changes as an atrophic metamorphosis consequent upon the suspension of the trophic influence transmitted through these nerves, but the correctness of this explanation is made doubtful by the experiments recently published in "Vratsch." A number of young animals were forced to daily violent exercise of some duration; they were killed at different periods, and it was found that under these conditions the heart became hypertrophied at first, while later on it became dilated and atrophied through fatty degeneration of the muscular fibers.

We meet with excessive cardiac action under a variety of conditions. It takes place in *exophthalmic goître*. This disease presents numerous features suggesting the propriety of the use of ergot, and yet I have met with only one mention† of its use resulting in the cure of the patient. I have had an opportunity to treat a typical case; the sedative action on the heart was very marked, but some time elapsed before the parts resumed their normal aspect.

* Inaug. Diss., St. Petersburg, 1879.

† "Allgem. med. Centr.-Zeitg.," 1878, No. 11.

The same excessive cardiac action occurs also in other purely nervous disorders, leading to hypertrophy first and to atrophy subsequently, and ergot should be used here also. These cases of *simple cardiac hypertrophy* have been treated frequently with ergot, and its action is well commented upon by Massini,* Arnal, Piedagnel, Sée, Gouillaud, and other French physicians,† Willebrand, and others. It is claimed that ergot can even reduce hypertrophy itself.

In the *valvular diseases* the hypertrophy is essential to keep the general circulation properly balanced; so long as the cardiac action does not exceed this demand its increased vigor is salutary. But, as everybody knows, very frequently there is a disproportion between the two, the action being either insufficient or too great. Digitalis will be of benefit in the first case, and will do harm in the latter; and it is such cases as fail to be relieved by digitalis that, according to Massini, are the proper ones to be treated with ergot. Timely use of this drug will tend materially to postpone the inevitable degenerative changes forming the third and the last stage in the evolution of cardiac valvular disease.

The possibility of the cardiac structure being relaxed, from an insufficient innervation, is gradually becoming recognized. This state would be analogous to the atony of other organs composed of the organic muscular tissue, with this difference, that in the heart the motility and the tonus are more sharply defined and are less dependent upon each other. The natural consequence of this defect will manifest itself by the so-called functional murmurs. Bamberger‡ assigns the majority of these inorganic murmurs to this cause. Rosenstein# distinctly states that with these murmurs it is not uncommon to find also temporary changes in the volume of the organ simulating a structural disease of the heart. Scheperln|| also ascribes anæmic cardiac murmurs to the valvular insufficiency due

* "Med. Record," 1878, p. 420.

† "Wien. med. Woch.," 1868, p. 126.

‡ Hoppe, "Postukivanie i Vislushivanie," St. Petersburg, 1866, p. 102.

Von Ziemssen's "Cyclopædia," vi, p. 55.

|| "N. Y. Med. Jour.," Nov., 1881, p. 469.

to dilatation of the heart. Immermann* is of the opinion that they are due to defective action of the mitral and tricuspid valves resulting from an atonic state of the papillary muscles. The fact that these murmurs are relieved by ergot,† the organ returning to its normal dimensions, would indicate very strongly that it acts not only upon the inhibitory innervation of the heart, but also as a cardiac stimulant. At least, Curran‡ found marked benefit from it in two cases of suspected fatty degeneration where cardiac action was particularly defective. He compares it favorably with carbonate of ammonium.

THE USE OF ERGOT IN VISCERAL ATONY.—There is a large number of diseases the essential feature of which is defective innervation of the organic muscular tissue entering into the composition of a given organ. Although in some cases this relaxed state is a secondary result of inflammatory action in the part itself, in the majority of cases we have to deal with primary atony and deficient innervation. Whatever may be the ultimate pathology in any given case, the usual practice consists in the use of various excito-motors, such as strychnine, electricity, douches, massage, etc. Considering that stimulation of the organic motor centers forms the most essential part of the physiological action of ergot, it is rather surprising that it is not used more commonly in these cases, particularly as ergot is superior to any other excito-motor.

Atony of the Stomach.—When dyspepsia is not due to the inflammatory and structural lesions of the stomach—in other words, when the patient suffers from *atonic dyspepsia*—the deficient innervation of the organ, glandular as well as motor, is accountable largely for the symptoms we are called to treat. We must bear in mind that the digestion, to be normal, depends not only upon the proper kind and quantity of the gastric secretion, but also upon the proper performance of the mechanical function of the stomach. To be well digested, the food must be thoroughly mixed with the gastric fluid, and the absorption of it depends largely upon the

* Von Ziemssen's "Cyclopædia," xvi, p. 399.

† "Edinb. Med. Jour.," Jan., 1877, p. 600.

‡ "Med. Press and Circular"; "Med. Record," 1870, p. 34.

active and constant movement of the contents against and along the walls of the stomach. That the motor function of the organ is defective in atonic dyspepsia, and to a greater or lesser extent in many other forms of the disease, we can readily infer from the co-existing, analogous conditions of other organs, and particularly from the concomitant intestinal atony.

The second indication for the use of ergot is *dilatation of the stomach*. The good results following the systematic pumping and cleansing of the gastric cavity clearly indicate that we have here, to a large extent, a paresis, and not simply a purely mechanical condition. The dilatation of the stomach, in fact, is mainly determined by the insufficient motor innervation, and is analogous to the uterine relaxation immediately after labor, and other like conditions elsewhere.

These two indications for the use of ergot are rational and consistent with the pathology of the diseases and the physiological properties of the drug. Yet I have failed to find a single allusion to its being used in these disorders. If ergot be administered by the rectum or hypodermically, there should be no fear of disturbing the digestion.

Atony of the Intestines.—This manifests itself mainly by *constipation*. This state of the bowels can be so readily acquired by irregular habits or a sedentary life, and it occurs so often in persons in delicate and enfeebled health, that there can be no doubt as to the cause of the condition. Belladonna is very frequently prescribed in constipation, but its physiological action can only aggravate the disease, as it paralyzes the motor innervation of the intestines. Ergot meets the main lesion so well that it should be used in all such cases. Its efficacy is well spoken of by those who have used it. Meadows (*loc. cit.*) finds it invaluable in cases of constipation occurring in children and women. Curran * succeeded in overcoming the torpidity of the bowels in paralytics when the most energetic purgatives had failed to act. Its power of increasing and causing peristalsis can be readily verified by the reader—let him take a full dose of the fluid extract of ergot, and within half an

* "Med. Record," 1870, p. 34.

hour he will notice the effects, varying from perceptible peristalsis to the actual inclination on the part of the bowels to move. Ergot should be used also in constipation following the prolonged administration of the narcotics, or succeeding peritonitis.

The relaxed state of the anal sphincters and of the rectal muscular tissue determines *prolapse of the rectum*. This is another instance of atony, and if the disease has not been allowed to assume a very grave form it is within the reach of remedies. Nux vomica and its preparations act well in these cases. Schwartz * speaks well of its local use. Langenbeck † was the first to suggest the use of ergot in rectal prolapse. His method of treatment consisted in hypodermic injections of ergotin (1–2 grs.) in the vicinity of the anus every few days, the parts being reduced and held there if necessary by some mechanical appliance. The results were very gratifying, and at times immediate. Semple (*loc. cit.*) reports successful results from like treatment. Steinbach ‡ cured three cases after having given six, seven, and eight injections respectively. The fourth case was only partially benefited, and had to be operated upon. A. H. Stephens (*loc. cit.*) refers to this treatment in the highest terms. In his paper he alludes to the successful cases of Vidal and others, published in the "Lancet."

Ergot has also been found of benefit in the *paralysis of the anal sphincter* occurring after parturition.*

Langenbeck (*loc. cit.*) obtained good results from using it hypodermically in *invagination of the rectum*.

Planat ‖ reports two cases of *strangulated hernia* reduced readily after hypodermic injections of ergot, although they had resisted unaided mechanical efforts.

Atony of the bladder, secondary to a diseased state of the spinal cord or due to a functional disorder of its innervation, invariably yields to ergot. Sutton ^ used it in the retention of urine occurring in the course of grave constitutional diseases—for example,

* "Nashville Jour. of Med. and Surg.," 1868.

† "Berl. klin. Woch.," 1873, p. 622.

* "Bull. Gén. de Thérap.," 1880, p. 358.

^ "Med. Record," 1879, ii, p. 48.

‡ Inaug. Diss., Berlin, 1876.

‖ "Gaz. des Hôp.," 1873, p. 1181.

typhoid fever. As a rule, the relief was very speedy, showing itself at times as soon as the physiological action of the drug had had time to manifest itself. Sorbet* cured a case of incontinence of urine, lasting fifteen years, in eleven days. Wernich recommends the use of ergot in all cases of incontinence of urine. Langenbeck† reported to the Berlin Medical Society three cases of atony of the bladder, occurring in connection with enlarged prostate, treated by hypodermic injections of ergotin. The contractile power of the organ increased very soon, so that the patients could expel the residual urine, and at the same time the enlargement of the gland became perceptibly diminished. Israel‡ reported a case in which the patient could not retain his urine for a longer period than ten minutes, but, after a brief course of treatment with ergot, the intervals between the micturitions increased to three hours. Clemens# found ergot of great value in the vesical atony of paralytics. Simpson|| reported a case of vesical atony of long standing cured after taking forty-five grains of ergot in one day. Malfese,^Δ Meadows, ◇ Spende, † Williams, ‡ Roth, ‡ Duhamel, Allier, Guersant, Payan, Arnal, Ritter, Houston, Girard,** and others, have all spoken favorably of the use of ergot in these disorders.

Atony of the Uterus and its Ligaments.—The atonic state of the uterine muscular tissue and its ligaments presents itself under two entirely different conditions. In one case we have to deal with feeble uterine contractions or their entire absence during labor. In the other, the relaxed condition of its structure and its ligaments determines displacements and flexions of the organ.

Not very many years ago ergot was used very frequently in obstetric practice; in fact, its action on the parturient uterus was

* "Gaz. des Hôp.," 1869, No. 18.

† "Berl. klin. Woch.," 1877, p. 24.

‡ "Berl. klin. Woch.," 1877.

"Dtsch. Klinik," 1865, No. 27.

|| "Med. Press and Circular," Aug., 1868.

Δ "London Med. Record," May, 1878.

◇ "Practitioner," Sept., 1868, p. 161.

‡ "Brit. Med. Jour.," 1874.

‡ "Centralbl. f. Chir.," 1875, p. 218.

‡ "Dtsch. Klinik," 1870, pp. 173, 201, 221, 240.

** "Bull. Gén. de Thérap.," xvi, p. 359; xvii, p. 88; xxv, p. 89; xxvii, pp. 171 288; xxviii, pp. 236, 397; xxx, p. 146; xli, p. 100.

considered at that time as its most important property. But practice has taught us to use ergot in labor with extreme caution, on account of the possible danger to the child as well as to the mother. If the uterine contractions are feeble, it should be used in very small doses during the first two stages of labor, and it is much safer to recur to some of the other means at our disposal. It is not proper to administer the full dose of ergot until the child's head appears at the vulva. It is given then, at the close of labor, not so much to influence the latter as to insure firm contraction of the organ after it has relieved itself of its contents, and to guard against the possibility of hæmorrhage.

While our predecessors committed an error by using ergot too much and at the wrong time, we do the same by not using it enough and when its action might be of benefit. I refer to the use of ergot in the puerperal state. The frequent occurrence of uterine disease as the result of a previous gestation and labor is often ascribed to puerperal traumatism—lacerations, fistulæ, etc. As the former occur also when the latter are absent, we are led to the conclusion that we attach too much importance to the inhibitory influence of these accidents upon uterine involution. It has suggested itself to many that most cases of subinvolution are caused by factors within the uterus, and not without—that, if we had pursued the same policy adopted at the close of labor for a longer period, the frequency of subinvolution and subsequent uterine disease would diminish. Some advocate for this purpose electricity, while others recommend the use of ergot. Apostoli* is among the former. He claims that the systematic use of the faradaic current during convalescence can prevent the accidents arising from the insufficient efforts of the uterus to return to its normal condition. All this is undeniably correct, and his statement that electricity acts more promptly and energetically than ergot I am prepared to grant, as I have had some opportunities to estimate the relative merits of these two agents. On the other hand, the action of ergot is more permanent and continuous, and the combination of both will present additional advantages. Ergot has been used with this object in

* "Ann. de Gynéc.," 1881, p. 327.

view by a number of physicians—Flowers,* Love,† Sell,‡ Hil-dreth,# and others. Kersch|| states that this treatment will tend to lessen the frequency of puerperal inflammatory and septic diseases. Le Dirberdier[^] and others claim that ergot can arrest *after-pains*.

Ergot has been used to produce *premature labor*, but this is a very crude and inferior method in comparison with the mechanical measures. That the object can be accomplished is well known. Ramsbotham[◇] reported six successful cases. If *miscarriage* is threatened by uterine congestion, the judicious use of ergot may prevent this accident.

The foregoing indications comprise the uses of ergot in obstetric practice.

The relaxed state of the uterine muscular tissue and of its ligaments determines *displacements* and *flexions* of the organ. It is when the latter are due to this cause that the treatment gives the most satisfactory results. Ergot should be combined with the local use of electricity, douches, tonics, etc. Of course it is important to keep the organ reduced by the proper pessaries while the patient undergoes the treatment.

THE USE OF ERGOT IN INFLAMMATORY AND OTHER MORBID ENLARGEMENTS AND GROWTHS.—The benefit derived from the use of ergot in these cases depends upon its action on the blood-vessels nourishing the tumor or participating in the inflammation. If organic muscular tissue enters into the composition of the part, the effects are intensified, because the entire organ contracts, and the result of this mechanical action is to hasten the degeneration, disintegration, and final absorption of the morbid elements.

We have already alluded to the use of ergot in the vascular growths. The other indications are the different hypertrophies of the organic muscular tissue, the enlargements due to congestion, hyperæmia, and inflammation; finally, the connective-tissue and other growths. The latter constitute the least promising field of

* "St. Louis Med. and Surg. Jour.," xxxvii, 1877, p. 98.

† "Atlanta Med. and Surg. Jour.," March, 1877. ‡ "Med. Record," 1878, p. 396.

"Lancet," May 19, 1866.

|| "Memorabilien," 1873, p. 202.

[^] "Ann. de Gynéc.," 1876.

◇ "Med. Times and Gaz.," 1863, p. 680.

all, although there are a few instances of benefit claimed to have been derived.

Hypertrophies of the Organic Muscular Tissue.—They present themselves under a great variety of structural conditions, which materially affects the results of treatment. The part may be the seat of a circumscribed growth, or the latter may assume a diffuse form, or, finally, the entire organ may share in the enlargement. These tumors are composed largely of muscular tissue; in some cases the connective tissue predominates, and occasionally the growth suffers cystic, calcareous, or fibrous degeneration. Very frequently it is impossible for us to recognize the actual state of the tumor, and, as the action of ergot is determined by the peculiarities of its structure, we should not be hasty in estimating its value by the results obtained in any given case. Sometimes the cure is very rapid and complete, or the recovery may be slow. In many cases we obtain only partial results, and, finally, the treatment may fail entirely. Uterine fibroid tumors and prostatic enlargements are the growths in which ergot has been used most frequently.

The treatment of *uterine fibroid tumors* with ergot was first suggested by Hildebrandt * in 1871. He used it not for the purpose of controlling the hæmorrhage so common in this disease, nor with the object of facilitating the enucleation of the tumors, but to induce their atrophy and absorption. In the general works on gynecology the merits of the ergot treatment are very much underestimated, and operative measures are recommended as the only reliable methods of dealing with these growths. Realizing as we do the structural peculiarities which may place the action of ergot in the least favorable conditions, we are prepared to meet with failures partial or complete; but it would be an error to think that such is the result in the majority of cases. In a great many instances the failures have been due not so much to the remedy itself as to the mode of using it. As an example of this I can cite the experience of Jäger, who pronounced ergot inefficient because a few hypodermic injections of ergotin failed to cause an immediate cure. Ergot should be used systematically and for a very long time, if necessary, and if the patient bears it well.

* "Berl. klin. Woch.," June 17, 1871.

For the purpose of estimating the actual value of ergot in the treatment of uterine fibroid tumors, I have collected all the cases reported in the periodical literature within my reach. I have omitted all those in which the result was not definitely stated or in which ergot was used only as a preparatory measure to an operation. I have excluded also a large number of cases in which the tumor was expelled. According to the results of the treatment, 223 cases collected can be divided into six groups:

1. The tumor was completely absorbed (42 cases).
2. The tumor was expelled (9 cases).
3. The tumor was diminished in size and the symptoms were relieved (71 cases).
4. The tumor was not affected, but the symptoms were improved (51 cases).
5. Ergot was of no benefit at all (49 cases).
6. The patient died in consequence of the treatment (1 case).

The death was due to the interstitial injection of ergotin. We find, then, that ergot is useless in only one quarter of the cases, and, if we exclude Jäger's 17 cases, the total failures occurred in less than one sixth of the entire number (15 per cent.). In the remaining cases the disease was benefited to a greater or less extent. Radical cure was obtained in one fourth, a marked improvement was obtained in one third, and relief from the hæmorrhage in one fourth of the cases. Such results, obtained in patients that were not considered as adapted for an operation, and consequently in tumors of considerable gravity, demonstrate a very decided efficacy of the ergot treatment. The operation when it succeeds leaves nothing to be desired, but, unfortunately, such result is not an invariable one. The mortality of enucleating *per vaginam* is about ten per cent., and that of gastrotomy, with or without the removal of the entire uterus, is about thirty per cent. To estimate the mortality of the cases operated upon, I have used only the reports which have appeared during the past ten years, because the results have been much more favorable. It seems to me, then, that we operate too much, and in cases that could have been benefited by milder measures. The legitimate cases for operation are those that have

resisted the more conservative methods. The ergot treatment is one of these, and it should be combined with the use of other agents having the same action. The diet treatment proposed by Dr. Salisbury has been favorably commented upon by some of our leading gynecologists, but it has fallen into disuse. The *rationale* of the diet treatment rests upon the principle that the heterologous tissues have a lesser vitality than those which are the normal component parts of our body, and, consequently, when we deprive our system of the ordinary supply of the energy-developing food, by making the diet exclusively or largely nitrogenous, heat and energy will develop at the expense of the tissues of the body, and the tumor tissue will be one of the first to be consumed.

Electricity has also been used in the treatment of uterine fibroid tumors. Martin* treated his cases with a strong interrupted galvanic current. Four cases were cured, in four the tumor diminished in size and the symptoms improved, in one only the latter result was obtained, and in three no improvement was noticed. His cases were mostly those of large tumors involving the entire organ. Everett used the faradaic current. Three cases were cured, two by the tumor being expelled and one by its gradual atrophy; in the remaining six the tumor diminished in size, and in four of them it descended so as to make the operative removal very easy. Cheron† used the same treatment as Martin in forty cases, and, although his article does not contain details, he speaks highly of the results. I have used the faradaic current in three cases. In one the tumor, situated in the anterior wall of the uterus, was absorbed; in one the treatment gave only relief of symptoms, the tumor in this case having a cavernous structure (myoma telangiectodes, Virchow); in the third case, very soon after the beginning of the treatment, the patient died in uræmic coma, with the symptoms of septicæmia, and on post-mortem the tumor was found breaking down in the center. These three methods may be combined together, giving results superior to those obtained singly, and reducing the contingent of operative cases to the minimum. The details of the cases of the uterine fibroid tumors treated with ergot are condensed in the following table:

* "Ann. de Gynæc.," 1879, p. 250.

† *Ibid.*, p. 65.

	No. of cases treated.	Cured.	Tumor expelled.	Tumor dimin'd. symp. relieved.	Symptoms relieved only.	No improvement.	Mode of administration of ergot.	
Hildebrandt...	27	3	..	11	9	4	Hyp.	Berl. klin. Woch., June 17, 1871; Am. Jour. of Obst., Feb., 1875, p. 529.
Herman.....	18	2	13	3	H. and Mouth.	Met. Times and Gaz., 1879, i, pp. 614, 670; ii, pp. 29, 98.
Bendelsdorff...	4	4	..	H.	Berl. klin. Woch., 1874, p. 21.
Munster.....	2	..	1	1	"	Dtsch. med. Woch., 1877, Nos. 14, 15.
Seydel.....	1	1	..	"	Dtsch. Zeitsch. f. prakt. Med., 25.
Daly.....	1	1	"	
Schwenrigger...	1	1	H.	Berl. klin. Woch., 1876, p. 466.
Chroback.....	9	1	..	2	3	3	"	Arch. f. Gynäk., vii, p. 293.
Atthill.....	3	2	1	"	Irish Hosp. Gaz., Sept. 1, 1874.
Clay.....	1	1	"	Lancet, May 10, 1873.
Ashhurst.....	1	1	"	Trans. of the Col. of Phys. of Phila., July, 1873.
Keating.....	2	1	1	..	"	Arch. f. Gynäk., vii, p. 384.
Fehling.....	1	1	"	Boston Med. and Surg. Jour., July 29, 1875.
Miller.....	1	1	1	..	M.	Arch. f. Gynäk., xiii, p. 182.
Leopold.....	12	4	5	3	H.	<i>Ibid.</i> , xiv, p. 494.
Reistadt.....	1	1	"	Obstet. Gaz., 1879, p. 433.
Stevens.....	1	1	M.	Practitioner, 1879, p. 31.
Renton.....	1	1	..	Rectum.	Lancet, 1879, i, p. 367.
Bell.....	3	1	1	1	"	Brit. Med. Jour., Sept. 2, 1876.
Atthill.....	2	1	1	..	H.	Med. Record, Jan. 20, 1875.
Collins.....	1	..	1	M.	Volkmann's Samml. klin. Vortr., No. 98, p. 763.
Winckel.....	8	5	2	1	H.	Med. and Surg. Report, Mar. 28, 1874.
Curry.....	2	2	R.	Chicago Med. Jour. and Ex., July, 1877.
Steele.....	3	1	2	H.	Amer. Jour. of Obstet., 1877, p. 470.
Anderson.....	1	1	"	Brit. Med. Jour., May 18, 1878.
Williams.....	2	2	H.	Trans. of the Am. Gynec. Soc., 1876, p. 168.
Byford.....	2	2	M.	<i>Ibid.</i> , i, p. 168.
Goodell.....	2	1	..	1	"	Arch. f. Gynäk., v, p. 169.
Hennig.....	1	1	H.	Amer. Jour. of Obstet., 1876, p. 301.
Parvin.....	3	3	..	"	Trans. of Minn. Med. Soc., 1879, p. 95.
Everts.....	1	..	1	"	Centralbl. f. Gynäk., 1879, p. 433.
Fritsch.....	1	..	1	H.	Edinb. Med. Jour., 1879, p. 260.
Simpson.....	1	..	1	"	Phila. Med. Times, Jan. 24, 1878.
Brubecker.....	2	..	2	"	Am. Jour. of Obstet., 1878, p. 351.
Ruge.....	1	1	"	Boston Med. and Surg. Jour., Jan. 24, 1878.
Dean.....	1	1	M.	Arch. f. klin. Chir., xx, p. 48.
Israel.....	1	1	..	H.	Inaug. Diss., Berlin.
Jäger.....	17	17	"	Centralbl. f. Gynäk., 1878, p. 485.
Heurteux.....	1	"	Edinb. Med. Jour., Jan., 1878.
Simpson.....	1	1	"	Przeglad Lek, 1878, No. 20.
Swidersky.....	2	2	"	Trans. Obst. Soc. of Lon., 1878, p. 282.
Brunton.....	1	1	M.	Am. Jour. of Med. Sci., 1880, p. 436.
Cushing.....	1	1	"	<i>Ibid.</i> , 422.
Jacobi.....	1	..	1	H.	Pacific Med. & Surg. Jour., xxiii, p. 399.
Pratt.....	1	1	"	Med. & Surg. Report, 1880, p. 512.
Marsh.....	1	1	M.	Trans. of Penn. Med. Soc., xiii, p. 65.
Goodell.....	1	1	"	Schmidt's Jahrbücher, clxxxvi, p. 95.
Wieden Hospital	1	1	H.	Clin. Lec. on Dis. of Wom., 1880, p. 132.
Duncan.....	1	1	H. & M.	Glasgow Med. Jour., 1879, p. 464.
Leishman.....	1	1	..	H.	Med. & Surg. Report, 1879, xli, p. 486.
Ferrell.....	1	1	M.	Arkansas Med. Monthly, 1880, p. 209.
Cross.....	5	1	..	4	H. & M.	Jour. de Méd., de Chir. et de Pharm., lxx, p. 341.
Liebrecht.....	4	1	..	1	..	2	R.	Tr. of the Am. Med. Ass., 1875, p. 173.
Byford's Collec'n	58	18	..	26	3	11	H. & M.	

Uterine hypertrophy, in the proper meaning of the term, is a very rare disease. Ergot can be tried with some hope of benefiting the patient.

Having spoken of the use of ergot in obstetric practice and in certain diseases of the uterus, to complete the subject it remains to say a few words on ergot in ordinary gynecological therapeutics. Although every case of uterine disease presents some special feature and some one lesion more prominent than the others, it can be said in a general manner that in the great majority of cases we have to deal simply with the modifications of one and the same condition—namely, abnormal nerve and blood supply. These two factors are, as a rule, intimately associated together, and, according to the manner in which they are combined and the intensity of each, we obtain a variety of clinical conditions, differing from each other as such, but having in common the same ultimate lesions. As a result of this, the indications in the treatment of the uterine diseases are essentially the same; we try to restore the organ to its proper place and to make it resume its normal form, and we attempt to relieve the congestion, hyperæmia, and inflammation. One or more of these indications is present in nearly every case, and, as ergot has a very decided influence upon the innervation and the blood supply of the uterus, we are led to conclude that its use will be advantageous in a great variety of conditions clinically dissimilar. A number of physicians have been induced by such considerations to use it quite frequently in their practice, and the results confirm the soundness of the reasoning.*

Embryologically, the prostate gland corresponds to the uterus, and when fully developed they present many common traits in health as well as in disease. *Enlargement of the prostate* in many respects is a condition analogous to uterine fibroid tumor. The main point of interest in connection with this disease is the interference with micturition and the subsequent disorders of the bladder. Langenbeck states that ergot not only relieves the latter,

* Swidersky, "Berl. klin. Woch.," 1870, p. 608; Leopold, "Arch. f. Gynäk.," 1878, p. 182; Garleitschenko, "St. Petersb. med. Woch.," 1876, No. 10; Meadows, "Practitioner," 1868, p. 161; Trousseau, "Wien. med. Woch.," 1868, p. 124, etc.

but also diminishes the enlargement. Atlee* obtained similar results. Riess and Guterback† were not able to confirm their experience.

The action of ergot in the *inflammatory enlargements* is due to its influence upon the morbid process itself. We have seen that it has been found useful in adenitis, orchitis, amygdalitis, mammary indurations, uterine enlargements, etc.

Outside of the above-named cases, ergot has been used very rarely. I will simply mention that Upsher‡ cured a very obstinate case of *villous growth of the rectum* with ergot suppositories. Spitzer# cured a number of cases of *nasal polypi* by ordering the patients to snuff powdered ergot. *Goîtres* have been treated and cured with it.¶ Dabney speaks of the good effect of ergot on *pterygium*. Crocket^ states that hypodermic injections of ergot dispersed a *recurrent mammary tumor* (the tumor previously removed was of a malignant nature). We can hardly expect much benefit from this drug in this class of tumors, because their dependence upon the blood supply in general is not very great.

The action of ergot on the enlarged spleen is of a greater practical and theoretical importance. It has been used quite frequently in *splenic leucocythæmia*, but the results were not favorable. Da Costa◇ states that he benefited two cases, but it is doubtful if they were cases of leucocythæmia. Much more certain is its action in the *malarial enlargements*, which rapidly disappear when it is given internally or hypodermically (in the usual manner or into the organ itself). The diminution in the size of the spleen is followed by improvement in the general condition of the patient.‡

Ergot has been used in two diseases, and apparently with such

* "Med. and Surg. Reporter," May 18, 1878.

† Virchow u. Hirsch, "Jahresb.," 1878.

‡ "Med. Record," 1879, p. 563.

"Gaz. Méd. de Paris," 1854, p. 478.

¶ Coghill, "Lancet," Aug. 4, 1877; Crocket, "Am. Jour. of the Med. Sci.," July 1876; Hammond, "Arch. of Clin. Surg.," Oct., 1876, etc.

^ *Ibid.*

◇ "Am. Jour. of the Med. Sci.," 1875, p. 117.

‡ Semple, *loc. cit.*; Miller, "Med. Record," 1876, p. 284; Hammond, "Trans. of the Am. Neurol. Assoc.," 1875, p. 142; Crocket, *loc. cit.*; Jones, "Med. and Surg. Reporter," 1876, p. 291.

good results that it deserves a mention. I refer to *malarial and typhoid fevers*. I bring up this subject here, because the action of ergot in these diseases can be explained only from the stand-point that the infection is localized in the spleen, which, in consequence of this, enlarges, and ergot, by reducing the latter, affects favorably the infected state of the system. The relation of the spleen to infection is so large a subject that I will refer the reader to the excellent papers on acute splenic enlargements by Mosler* and Wardell,† also to the paper of Hertz‡ on malaria, where all that is known is fully stated. I will call his attention to a theory which is rapidly gaining favor in the profession—namely, that the spleen, by its peculiar position in the circulatory system, and by its peculiarities of structure, serves as a filter and reservoir in which the germs of poison causing the disease are detained. The latter act as an irritant, and the organ enlarges in consequence. It is a significant and well-established fact, that all measures tending to reduce this splenic swelling exert also a favorable action upon the disease itself. This statement is applicable only to malaria, but the same may prove true also with regard to other infectious diseases. “I should not like to deny that the action of quinine in malarial fever may be attributed *in part* to its influence in reducing the size of the spleen, as other remedies which act in the same way on the spleen, such as eucalyptus globulus, gentianin, strychnine, the use of cold water, etc., have a reputation as febrifuges.”#

The beneficial action of cold douches, general or local, over the region of the spleen, is well established. Some go so far as to claim that they are superior to other methods of treating the disease. This is unquestionably an exaggerated statement, but it teaches that a measure purely mechanical, and having no other property but to stimulate the spleen, can cure the disease. From this stand-point the results obtained by Schröder|| with faradization of the spleen in malaria are very interesting. He treated in this manner

* Von Ziemssen's "Cyclopædia," viii, p. 450.

† Reynolds's "System of Medicine," v, p. 139.

‡ Von Ziemssen's "Cyclopædia," ii, p. 643 *et seq.*

Hertz, *op. cit.*, p. 668.

|| "St. Petersb. med. Woch.," 1879.

forty-two patients suffering from recent or long-standing malarial intoxication. The result was as follows: If on the eve of the expected paroxysm the spleen was faradized, the occurrence of the attack was prevented in the majority of cases, and a course of such treatment was sufficient alone to cure the disease. In thirty-nine cases the cure was complete and permanent, in two cases the malaria returned when the treatment ceased, and in only one case no benefit was derived. The analogy between cold and electricity is an absolute one, and their favorable action can be explained only by their causing the spleen to contract and to expel into the circulating blood the poison retained in the organ, where it perishes more rapidly, as it is a less favorable medium than its former abode. It is natural, then, to expect also similar results from ergot, which acts on the enlarged spleen in a very decided manner. Deboné,* having observed some points of resemblance in the physiological actions of quinine and ergot, attempted to test the identity of their action by using the latter in the treatment of malarial fevers, which in the valley of Pau are very severe. He reported fourteen cures and only one failure. A. Jacobi † has used ergot in the same disease during the past twelve years, and he considers it a very active remedy, frequently curing the disease when quinine has failed to act. All these facts show clearly that the spleen stands in a very intimate relation to infection, and that the remedies acting upon it cure the disease, very likely by dislodging the poison from it and forcing the latter into a sphere less suited for its maintenance.

The facts relating to the treatment of typhoid fever with ergot sustain this view. Deboné ‡ used it in fifteen cases, of which number seven were mild and eight severe. Two patients died, but the drug that was given them was afterward found inert. He was very much pleased with its action, but the details are not given. He states that the same treatment was adopted by Billard twenty years before him, but with what success and on what ground was not stated. Hayem's § account is more complete. He considers

* "New Remedies," 1874, 1, p. 300.

† "Med. Record," Oct. 1, 1870.

‡ "Gaz. Hebdom.," Sept. 1, 1870.

§ "Am. Jour. of the Med. Sci.," 1876, 1, p. 56.

the antipyretic properties of ergot superior to those of digitalis and quinine, and, according to him, patients do much better on ergot than on the latter two substances. The defervescence occurs at an earlier date, and the fever runs a milder course. If ergot is given during the day, the evening temperature is lower than that of the morning. It is very desirable to have more facts with regard to the action of ergot in these diseases.

THE USE OF ERGOT IN ABNORMALITIES OF SECRETION OF THE GLANDS AND THE MUCOUS MEMBRANES.—When a gland is in a state of functional activity its blood supply is more active, and its innervation is in a state of irritation. In disease, when its activity is excessive, we have essentially the same elements to deal with, only on a larger scale. Some of the remedies which increase or suppress the secretions do so by acting on the glandular nerve centers. Such are atropine, opium, and pilocarpine. Their peculiarity is, that they produce their specific effects in health as well as in disease, and that they influence only certain glands, having no relation whatever to others. Ergot differs from them. Its action in health is imperceptible, while it has a very wide range of action in disease. These differences naturally suggest the idea that ergot acts mainly upon the circulation, and in a lesser degree if at all on the glandular innervation. Its action is particularly marked when the vaso-motor disturbance predominates, as is the case in diabetes insipidus and intestinal fluxes.

The excessive mucous or muco-purulent discharge is due to inflammation or to a relaxed state of the blood-vessels of a given mucous membrane. Ergot diminishes it by acting upon the circulation of the part.

Ergot promptly checks excessive flow of *milk*, and is capable of suppressing it entirely. It acts in this manner also on animals.* It should be used when the mammary gland becomes swollen and inflamed in consequence of weaning the child or from any other cause.

* Le Gendre, "Jour. de Chem. Méd.," Oct., 1869, p. 475; Payet and Cammormond, "Schmidt's Jahrbücher," cxxii, p. 180; Scherebenikoff, *loc. cit.*, etc.

Christmann* and Abrendt† found ergot very useful in cases of excessive *perspiration*, and particularly in hectic sweat.

Diabetes insipidus, which is due to paresis of the renal vasomotor apparatus, is almost always cured with ergot.‡ It is essential to use ergot in as large doses as the patient can bear, and the treatment must not be abandoned too soon. *Diabetes mellitus* is a graver and more extensive morbid condition, but ergot is of great service here, also, although in a lesser degree.⁴

Sœquet and Chalin‖ have used ergot in *albuminuria*. Their patients were benefited. The albumen gradually disappeared from the urine, and the dropsical phenomena passed off. Perroud⁵ regards this treatment as symptomatic and not curative. We can not expect much benefit in the advanced stages of the disease, but recent cases of kidney disease present a promising field for further study.

Spermatorrhœa is a purely nervous disease; still it can be considered here, as is the customary practice. Impotence, of which spermatorrhœa is only a symptom, is characterized by an excessive irritability of the reflex centers situated in the lumbar spine, and governing the act of ejaculation. This condition is due partly to their functional over-use and partly to a congested state of the lumbar portion of the spinal cord. During the night, when the inhibitory function of the brain is suspended, any peripheral irritation in the domain of the genito-urinary apparatus may be sufficient to determine a seminal emission. The fact that it usually occurs during the early morning is due to the bladder being distended with urine, and to sleep being particularly deep at that time. When we use ergot in these cases we must not expect everything from it, and it should be combined with sedatives, tonics, and particularly with local and general electrization. Ergot will relieve

* "Centralbl. f. d. med. Wissensch.," 1869, p. 800.

† "Berl. klin. Woch.," 1873, p. 539.

‡ Da Costa, "Med. News," Jan. 7, 1882, p. 5.

⁴ Shearer, "Med. and Surg. Reporter," March 16, 1872; Foster, "Brit. and For. Med.-Chir. Rev.," Oct., 1872; Hasse, "Schmidt's Jahrb.," clxxv, etc.

‖ "Brit. and For. Med.-Chir. Rev.," Jan., 1864.

⁵ *Ibid.*

the congestion of the spine and at the neck of the bladder; it will also tone up the blood-vessels of the urethral mucous membrane. It has seemed to me frequently as if ergot had the power of stimulating the sexual centers.

Prostatorrhœa is another symptom of impotence. It is due to congestion of the prostate gland, which results in a catarrhal condition of the follicles, sometimes quite severe. Ergot will relieve this symptom, as well as all other vascular disorders peculiar to this disease.

In speaking of the use of ergot in inflammations of the mucous membranes, it was stated that it benefited *leucorrhœa*,* *cystitis*,† *bronchitis*, *conjunctivitis*, *pharyngitis*, *nasal catarrh*, *gleet*, and *gonorrhœa*. In urethral inflammation Curran‡ used injections of ergot, while Eldridge (*loc. cit.*) made use of urethral bougies. Negri* administered ergot internally during the chronic stages of gonorrhœa, in men as well as in women.

Hampel|| and Griepenkerl^ found ergot useful in *whooping-cough*. Eulenburg◇ states that it acts as a neurotic by diminishing the irritability of the laryngeal mucous membrane.

The use of ergot in *diarrhœa* and *dysentery* is of considerable practical importance. In diarrhœa the benefit will be in proportion to the intensity of the vaso-motor disturbance. If it is due simply to heightened peristalsis, ergot will be useless, and we should prescribe opiates after we have removed the offending cause. In purely inflammatory diarrhœa ergot will be of service, but in a lesser degree than in mere functional vaso-motor disturbances. The latter occur much more frequently than is generally admitted. The occurrence of diarrhœa is imputed, as a rule, to the existence of a catarrhal condition of the intestinal mucous membrane. That this is not the case, we infer from the fact that diarrhœa is seldom a febrile disease; constitutional symptoms hardly ever occur, and

* See the literature relating to the use of ergot in gynecological practice.

† See the literature relating to the use of ergot in vesical atony.

‡ "Med. Record," 1870, p. 34. * Pereira, "Materia Medica," 1854, ii, p. 141.

|| "Allgem. wien. med. Zeitung," 1868, No. 19. ^ "Dtsch. Klinik," xv, pp. 134, 146.

◇ "Berl. klin. Woch.," 1869, p. 118.

the evacuations are profuse and watery, containing a very slight percentage of albumen or none at all. The latter feature is very suggestive of a pure vaso-motor disturbance, and speaks strongly against the inflammatory nature of the disease. If we bear in mind the anatomical peculiarities of the intestinal canal, we can readily understand how a mild vascular tension can cause a very profuse diarrhœa. The veins are intimately attached to the muscular tissue, and pierce the latter at an acute angle, so that an active peristalsis, by interfering with the circulation in the veins, will lead to a rise of the arterial tension. The venous blood, before it empties into the vena cava, must first pass through the close network of the hepatic capillaries, a condition hindering a rapid establishment of the equilibrium in case of sudden determination of blood to the intestinal blood-vessels. Finally, according to recent researches, the capillaries of the intestines are particularly prone to furnish an abundant transudation of serum.* We can readily perceive how a profuse diarrhœa may occur from a purely functional vaso-motor disturbance; and it should be treated with ergot in connection with opiates, because the only indications present are to relieve the irritation and to quiet the circulation. In inflammatory diarrhœa the passages assume a character distinctive of a catarrhal condition; they contain mucus or muco-pus, they are less abundant and less watery, and the disease presents also a peculiar history. Ergot is of service also in this variety of the disease. The literature relating to the uses of ergot in diarrhœa is very abundant, and it is in general highly commendatory.†

Ergot has been used also in dysentery, and with very good results.‡ Its mode of action is essentially the same as in diarrhœa.

THE USES OF ERGOT IN DISEASES OF THE NERVOUS SYSTEM.—

* Cohnheim and Liechtheim, "Arch. f. path. Anat. u. Physiol. u. f. klin. Med.," lxi, p. 106.

† Massolez, "Gaz. des Hôp.," Dec. 16, 1856; "Comptes Rendus," xliii, p. 7; Rillet, Lombard, Jonkyrat, "Wien. med. Woch.," 1865, p. 451; Gross, "Allg. wien. med. Zeitung," 1868, No. 25; Comegys, "Louisville Med. News," 1876, p. 135; Lutton, "Gaz. Hebdom.," 1872, No. 38, *et seq.*

‡ Gross, *loc. cit.*; Barlan-Fontayral, "New Remedies," 1872, p. 246; Clark, "Med. Times and Gaz.," 1862, p. 124; Gervis, "Bull. Gén. de Thérap.," 1847, pp. 163, *et seq.*

In making a distinct group of these diseases, I am prompted to do so, not because ergot acts here in a manner different from what we have already seen, nor because they present lesions peculiar to themselves. The nervous system responds to the vascular disorders within it more readily than any other organs or tissues, producing a great variety of symptoms, which have been treated with ergot more frequently than others. Consequently a review of the results obtained is important, as it illustrates admirably the therapeutic value of ergot in the treatment of these morbid conditions. It remains only to extend the use of ergot to other departments of special pathology, in which the results will be as gratifying as in the domain of nervous affections.

Ergot is the standard remedy in the inflammatory diseases of the cerebro-spinal axis. The diseases of the spinal cord and its membranes, being the more common, have been treated with ergot more frequently, and the general experience is to the effect that it is a very valuable and active agent in these cases. It is urged that we must not adhere too closely to the doses laid down in the books, but push the medicine as far as the patient can bear it safely and comfortably, and it is surprising how great the tolerance may be. It is generally advisable to combine ergot with iodide of potassium, in connection with the use of electricity, counter-irritants, cold, etc.

Ergot is used even more frequently in the diseases of the cerebro-spinal axis associated with or depending upon congestion and hyperæmia. Who is not aware of the rapid relief following its use in congestive headaches, congestion of the spine, and hyperæmia of the brain and cord?

Epilepsy has been treated with ergot, alone or combined with other remedies, and the results have been good.*

Jacobi† used it in a case of *chorea* caused by a hyperæmic state of the cord, and the patient made a rapid recovery.

* Yeats, "Med. Times and Gaz.," July 13, 1872; McLane Hamilton, "N. Y. Med. Jour.," 1875, p. 187; Baudney, "New Remedies," 1879, p. 178.

† "N. Y. Med. Jour.," 1865, p. 142.

Various forms of *insanity* are aggravated by cerebral hyperæmia, and ergot is very beneficial in these cases.*

Dedrickson † obtained good results in *sun-stroke* and its after-effects.

Ergot has been used with very good results in the different *vasomotor neuroses*—hemicrania of the vaso-paralytic type, ‡ and herpes zoster (Sachse).

When a neuralgia depends upon vascular disorders of the nerve sheaths, ergot is very frequently of great benefit. Woakes # was the first to adopt the hypodermic injections, made in the vicinity of the painful spots, or in indifferent parts of the body. His good results have been confirmed by others. || Still this mode of treatment is not very reliable.

Dr. Stites ^ recently published a very interesting paper on the use of ergot with iodide of potassium in *lead poisoning*.

It lies entirely with us to multiply the uses of ergot in this class of diseases, so long as there is an evidence of a vascular disorder being the cause of the symptom we wish to relieve.

In closing the subject it remains to call attention to the treatment of *rheumatism* with this drug. In two instances the practice originated by a mistake or by an accident; in the third the motive for using it was not stated—but in all cases its beneficial action was highly spoken of. I have had a limited experience with ergot myself, and find it very useful in a certain class of cases. In the present state of the pathology of rheumatism, it is inconceivable how ergot can affect the disease at all, and this is the reason why the recommendation of those who have used it has not been followed by others. It would be out of place to enter into a discussion of the nature of rheumatism; the subject is too large to be

* Mann, "N. Y. Med. Jour.," June, 1875; Kitchen, "Am. Jour. of Insanity," July, 1873.

† "Am. Jour. of the Med. Sci.," Oct., 1878.

‡ Schumacher, "Berl. klin. Woch.," 1876, p. 173; Eulenburg, *ibid.*, 1873, No. 15; "Lancet," Aug. 17, 1878; Marino, "Jour. of Ment. and Nerv. Dis.," 1879, 2, p. 157.

"Brit. Med. Jour.," Oct. 3, 1863.

|| Spence, "Brit. Med. Jour.," 1874; Marino, *loc. cit.*; Eldridge, *loc. cit.*

^ "Med. and Surg. Reporter," Nov. 19, 1881.

presented in the limited space at my disposal. It will suffice to say that none of the theories thus far proposed give us an intelligent account of the disease. The lactic-acid theory is rapidly losing its former prestige. The miasmatic theory, which is of more recent origin, is even less tenable. The humoral and infectious principles failing to satisfy the requirements of the disease, our mind naturally turns toward the nervous system. The origin, symptoms, and complications of rheumatism, the character of the agents that have an undoubted curative action, all point toward the principal lesion being in the spinal cord. We can go even so far as to assume the existence, in the acute forms of the disease, of a hyperæmic state of a certain region of the cord. From this stand-point—and I regret that I can not present it here more fully—we can readily understand how ergot may have a very decided action on the course of acute rheumatism. Gillette (père)* was the first to test the value of our drug in this disease. He was led to use it after having observed a very marked improvement in a rheumatic patient who had taken a number of doses of ergot which was given him by mistake instead of quinine. As the result of an extensive experience, he pronounces ergot a very valuable remedy. He claims that the first effect is to quiet the circulation, when the joint symptoms rapidly subside. The reports of fifteen cases confirm this claim. For the details I have to refer the reader to the original paper.

Evan M. Boddy† has also used ergot very frequently, and he regards its employment as superior to any treatment thus far used. It lowers the temperature, the duration of the disease is shortened, the liability to cardiac complications is diminished, and when they are present they are very much benefited by it.

Chevallereau‡ administered a hypodermic injection of ergotin to a rheumatic patient to stop a hæmorrhage. It acted also so well on the rheumatic symptoms that he persisted in this treatment, and

* "Rev. de Thérap. Med.-Chir.," 1874, p. 455.

† "Med. Press and Circ.," 1877, i, p. 298.

‡ "France Méd.," Nov. 14, 1880; "Allg. wien. med. Zeitung," Jan. 4, 1881.

used it in two other cases. In all these three patients the benefit was very striking.

In all these cases ergot was used in acute articular rheumatism. My own experience has been limited to apyretic subacute rheumatism and to patients convalescing from more acute forms of the disease—consequently to cases less adapted to the ergot treatment—but its use has been followed by good results, and in proportion to the severity of the symptoms.

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